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Recurrent respiratory papillomatosis complicated by aspergillosis: A case report with review of literature

Kuruvilla S, Saldanha R, Joseph LD

ABSTRACT
Pulmonary extension of recurrent invasive papillomatosis often poses a diagnostic challenge to the examining bronchoscopist, pathologist, radiologist and surgeon, in distinguishing it as a benign lesion that is confined to the mucosa and extending along the branches of the tracheobronchial tree from true invasion of a malignant tumor. We document here a case of recurrent invasive respiratory papillomatosis which initially presented as a laryngeal papilloma. After multiple recurrences, the patient presented with bronchopulmonary involvement, complicated by invasive aspergillosis in a non-immunocompromised setting.

KEY WORDS: Aspergillosis, bronchiectasis, papillomatosis

Case Report

Recurrent respiratory papillomatosis (RRP) is a disease of viral etiology and is a benign self-limiting disease, characterized by recurrent proliferations of benign squamous papillomata within the larynx. The trachea, bronchi and proximal bronchioles are involved in 2-26% of the cases, whereas the lungs are involved in less than 1% of the cases.[1] Intrapulmonary extension of laryngeal papillomatosis is often complicated by pneumonia or bronchiectasis, with superadded bacterial or fungal infections. Occasionally, it may be aggressive and rarely undergoes malignant transformation.

A 13-year-old male patient presented with massive hemoptysis for three months, breathlessness on exertion and hoarseness of voice. He gave a history of human papilloma virus infection of the vocal cords since the age of three years, for which he underwent ablation seven times.

CT scan [Figure 1] showed a cavity with a mural/intraluminal nodule, possibly an aspergilloma. The nodules seen around the cavity could be ectatic bronchi with secretions. There was evidence of a papillomatous lesion in other views of the CT.

A left lower lobectomy was performed and the lesion was predominantly seen in the superior segment of the left lower lobe. The lobectomy specimen weighed 110 g. Cut surface showed a cavitary lesion measuring 1.5 cm adjacent to which was seen, a grey-brown papillary tumor measuring 2 x 0.5 cm.

The tumor appeared friable and necrotic. Microscopy showed extensive squamous papillomatosis arising in ectatic bronchi and bronchioles, with extension into the adjacent lung parenchyma. However, the basement membrane appeared intact and there was no evidence of true invasion. The tumor cells appeared squamous in nature with vesicular nuclei and abundant eosinophilic cytoplasm. There was no nuclear atypia. The bronchi and bronchioles showed bronchiectatic changes with extensive chronic inflammation and squamous metaplasia. There was an adjacent cavitary lesion containing a fungal ball consisting of numerous hyphae with acute angle branching resembling Aspergillus [Figure 2]. Fungal hyphae were also seen invading the underlying lung [Figures 3 and 4]. The rest of the lung showed patchy areas of pneumonic consolidation.

The final diagnosis was given as invasive papillomatosis (intrapulmonary spread from a laryngeal papilloma) in a bronchiectatic lung with aspergilloma and early invasive aspergillosis. The treatment modality adopted in this case was surgical resection followed by antifungal treatment with Itraconazole 200 mg twice daily for three months.

Discussion

Juvenile laryngeal papillomatosis is caused by the human papilloma virus Type 6. More than 60 subtypes of human papilloma virus exist, but the most important implicated agents are 6 and 11. This lesion is characterized by recurrent proliferations of benign squamous papillomata within the
respiratory tract. Histologically, the papillomata consist of multiple finger-like projections with a central fibrovascular core, which is typically covered by stratified squamous epithelium. Although benign histologically, respiratory papillomatosis may behave aggressively and can precipitate sudden airway obstruction. They clinically present with hoarseness of voice and aphonia, repeated episodes of respiratory distress and recurrent pneumonia. In addition there can be associated inspiratory stridor, asthma-like symptoms and hemoptysis. Loccit Pulmonary papillomatosis usually occurs 10 years after the initial diagnosis and malignant transformation into an invasive squamous cell carcinoma and adenosquamous carcinoma have been reported. Molecular markers of transformation include increased topoisomerase alpha II and p53 expression along with RB gene protein product and p21 expression.

The most common site of involvement by respiratory papillomatosis is the true vocal cord, followed by the trachea, bronchi, palate, nasopharynx and pulmonary parenchyma. Pulmonary lesions include nodule formation, atelectasis, pneumonia, bronchiecstasis, cavitations and carcinomatous transformation or may even be fatal. Glikman et al. reported the case of a five-year-old female who presented initially with respiratory papillomata in the larynx and trachea and following treatment with alpha-Interferon, developed pulmonary lesions with cavitation, 16 months later and died of pneumonic complications.

It is believed that aggressive RRP may lead to iatrogenic airway stenosis as a result of frequent surgical procedures. Tracheotomy done in such a situation has been implicated in the progression of RRP to distal airway disease. This could have occurred as a consequence to tracheal trauma as is evident in this study.

Respiratory papillomatosis could be of the juvenile or adult onset type. Juvenile onset disease is transmitted vertically from a mother with active human papilloma virus (HPV) lesions in the genital region or latent infection transmitted to the newborn via the birth canal. Adult onset respiratory papillomatosis occurs usually due to reactivation of the HPV virus present...
since birth. The other possible mode of spread is by sexual transmission. Compared to juvenile onset recurrent respiratory papillomatosis, which is more aggressive, adult onset lesions are single and recurrences are rare.

Rabah et al. [8] have shown that human papilloma virus typing is a useful diagnostic marker for aggressive recurrent laryngeal papillomatosis and there was no correlation of proliferative indices Ki 67 or p53 with the clinical behavior.

The peculiarity of respiratory papillomatosis is that although it is biologically confined to the mucosa, to the histopathologist it gives the initial impression of a very well-differentiated squamous cell carcinoma with satellite islands of tumor tissue. This is due to the fact that intramucosal extension along the bronchial and bronchiolar mucosa into the distal and more terminal bronchioles gives an impression of aggressive behavior, however, careful examination would reveal an intact basement membrane with no microscopic evidence of invasion.

Invasive pulmonary aspergillosis usually occurs in immunocompromised individuals [9] and may occur as complications of cavitary lesions, tuberculosis and bronchiectasis or lung neoplasms. Invasive aspergillosis has also been reported [10] to occur in immunocompetent hosts with chronic obstructive lung disease even in the absence of risk factors such as corticosteroid or cytotoxic therapy, use of broad-spectrum antimicrobial agents, severe granulocytopenia or qualitative granulocyte defects. In such situation, a clinical suspicion of aspergillosis arises, particularly if there is lack of responsiveness to routine antimicrobial drugs.

Infectious complications of RRP have been known to occur. However, there is no previous report in the literature of aspergillosis complicating RRP with bronchiectasis and intrapulmonary extension and particularly so in an apparently immunocompetent individual, which is the unique feature of this case.

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