Acta Otorrinolaringol Esp. 2018;69(2):110–113

Acta Otorrinolaringológica Española

www.elsevier.es/otorrino

CASE STUDY

Recurrent Respiratory Papillomatosis With Lung and Chest Wall Involvement: A Rare Complication in an Adolescent☆

Papilomatosis respiratoria recurrente con compromiso pulmonar y de la pared torácica: una rara complicación en un adolescente

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Received 14 November 2016; accepted 5 December 2016

Clinical Case

A 15-year-old male patient, diagnosed with laryngeal papillomatosis at the age of 5 that progressed to tracheal and bronchopulmonary spread at the age of 11, attended the endoscopy department with serious respiratory difficulty, stridor and dysphonia. The patient had no other history of disease.

Physical examination revealed a round lesion with abundant papillomas on the posterior chest wall (Fig. 1).

The airway was assessed under general anaesthesia and papillomatous lesions were observed in the larynx, trachea and right main bronchus, which were resected with microforceps and microdebrider. Samples were sent for anatomopathological analysis.

A chest CT was performed showing a voluminous right paravertebral lesion of 10.6 cm × 9 cm × 8.8 cm (longitudinal, transverse, anteroposterior) extending from the pulmonary parenchyma dorsally towards the soft tissues. Multiple cavitating nodular formations were also observed in both lung fields, involvement of the right paraspinal muscles and the dorsal vertebral bodies from D2 to D7 with osteolytic areas and expansive osteolytic lesions at the level of the posterior arches of the sixth and seventh ribs on the right side (Fig. 2). Adenopathies of 1.5 cm were observed in the mediastinum.

☆ Please cite this article as: Rodríguez H, Cuestas G, Álvarez M, Monaje M. Papilomatosis respiratoria recurrente con compromiso pulmonar y de la pared torácica: una rara complicación en un adolescente. Acta Otorrinolaringol Esp. 2018;69:110–113.

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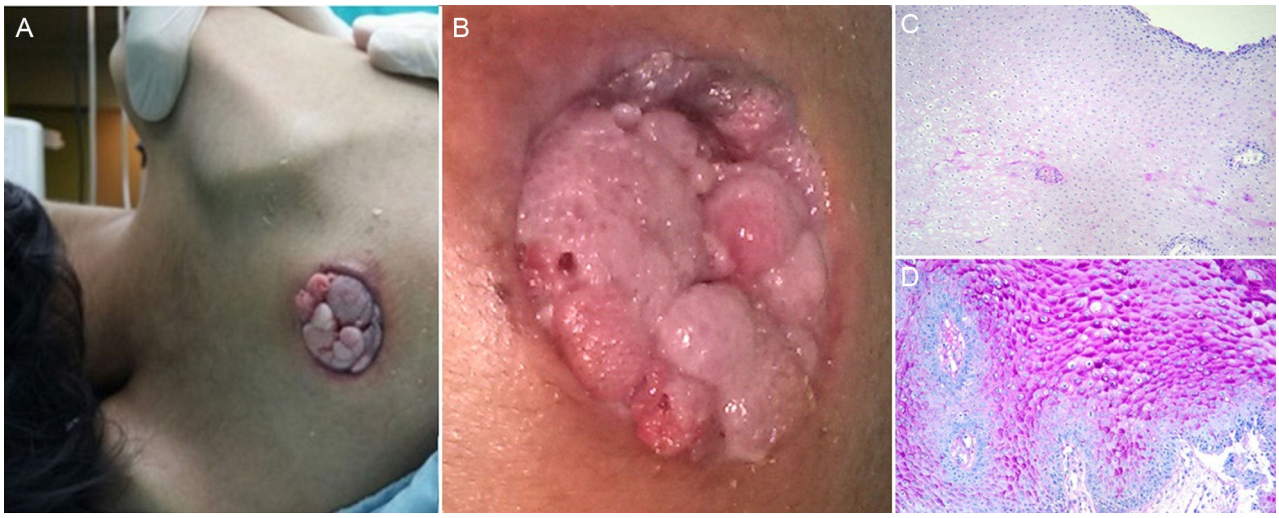

Fig. 1 (A) Fistulous lesion of the lung parenchyma in the posterior chest wall with abundant papillomas. (B) Enlarged image. (C) and (D) Histopathology of the chest wall lesion. The papillomas comprise finger-like projections with a central fibrovascular nucleus and stratified pavimentous epithelium. The presence of koilocytes is highlighted: epithelial cells with eccentric nucleus and vacuolated cytoplasm (paranuclear halo), which is the classical manifestation of human papilloma virus infection in the cell.

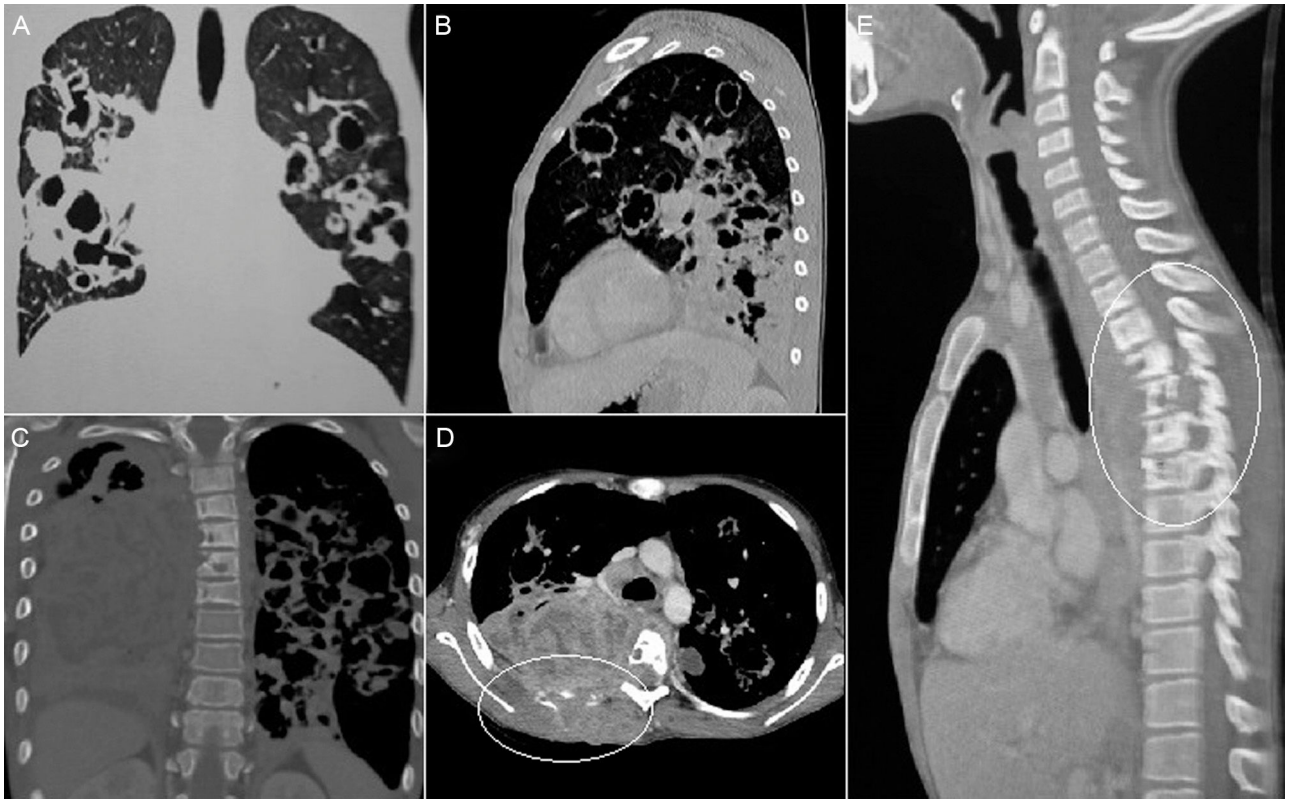

Fig. 2 Computerised tomography of the chest: (A) and (B) Cavitating nodular formations are observed in both lung fields. (A) Coronal slice. (B) Sagittal slice. (C) A voluminous lesion is observed in the right lung parenchyma. Coronal slice. (D) Involvement of the posterior rib arch (circle). Axial slice. (E) Involvement of the dorsal vertebrae (circle). Sagittal slice.

Bronchoalveolar lavage, transthoracic biopsy of the right lung parenchyma and biopsy of the chest wall lesion were performed.

The anatomopathological report confirmed the diagnosis of disseminated papillomatosis (Figs. 1C and D). None of the samples analysed showed cellular atypia or dysplasia. Viral typing was positive for the human papilloma virus (HPV) subtype 11.

From the age of 5, the patient had undergone multiple microsurgeries for recurrent papillomatosis and adjuvant medical treatment with interferon-α and intralesional cidofovir. Despite intensive treatment, the disease progressed, pulmonary involvement increased and spread to the chest wall.

Systemic treatment with intravenous cidofovir 5 mg/kg (5 doses, once a week) was given, with no clinical improvement. Systemic treatment with bevacizumab was suggested, but the family and the patient refused and decided to return to their home town. The patient died 2 months later.

Discussion

Recurrent respiratory papillomatosis (RRP) is a rare disease of the digestive tract and airway caused by HPV, principally types 6 and 11.[1,2] Its prevalence is estimated at between 1.45 and 2.93 per 100,000 children.[3] It is the most common benign neoplasm of the larynx in children.

Although a benign disease, its clinical course is unpredictable, there is a tendency to recur and spread (30% of children).[2] Morbidity can be significant and cause potentially fatal obstruction of the airway or progress to malignant neoplasia.

It most commonly affects the larynx. Tracheal involvement occurs in 8% and lung involvement in <1% of cases of RRP.[1,2] Lung involvement is most common in males and is associated with a more aggressive disease course and low risk of malignant transformation (1%–2%).[2,4] Spread to the chest wall, as in our patient, is very rare.

The age of onset of the disease is the most important factor for the prognosis of RRP; onset before the age of 3 years suggests an aggressive prognosis.[4,5] Tracheotomy facilitates spread.[6] The viral serotype also relates to the severity of the disease and its clinical course.

The presence of HPV 11 in papillomas is associated with more aggressive disease, diagnosis at an earlier age, significant obstruction, greater recurrence, higher risk of bronchopulmonary spread and the need for more frequent surgery.[4,5]

HPV 11 is the subtype identified in the documented cases of malignant transformation of lung lesions, which suggests that it might play an important role in the malignant transformation of RRP.[1,4] Other factors, such as the drugs used for treatment, X-rays taken throughout the disease, repeated lung infections and the host's immune response, might also be considered.[7] In general, the patients are male, diagnosed at an early age with considerable lung involvement of the RRP.[1]

A previous lesion that has increased in size, and the presence of mediastinal adenopathies should lead to suspicion of malignancy.[4]

Due to the aggressive progression of the disease in our patient, we suspected transformation to squamous carcinoma, but none of the anatomopathological studies confirmed this.

The available treatment, both medical and surgical, is palliative, aimed at maintaining the airway and achieving acceptable voice quality. Tracheobronchial lesions and lesions of the lung parenchyma that are not accessible to local intervention pose a major therapeutic challenge.

Although historically interferon was the most common adjuvant therapy, intralesional cidofovir is used more nowadays. However, successful outcomes are not achieved in all children, and the drug is not risk-free.[8] Its intravenous administration carries the risk of nephrotoxicity and neutropenia. Therefore, patients receiving the drug must be monitored for toxicity and adverse reactions.[2]

Vascularisation is a determining factor in how fast the papillomas grow. Vascular endothelial growth factor inhibition with bevacizumab appears to be a new and effective treatment.[3,8] Systemic bevacizumab might be a promising strategy in the treatment of RRP with tracheal and bronchopulmonary spread.[9,10]

The greatest hope lies in the quadrivalent vaccine against HIV subtypes 6, 11, 16 and 18, which holds the promise to reduce the incidence of RRP.

RRP is a relatively rare disease that can potentially fatally compromise the airway. Due to the disease's tendency to recur, its unpredictable course, extra-laryngeal spread and the risk of malignant transformation, meticulous monitoring of the RRP patient and viral typing are essential. The prognosis for RRP with intrapulmonary spread is poor.

Conflict of Interests

The authors have no conflict of interests to declare.

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