Clinical note

Utility of positron emission tomography with $^{18}$F-FDG in a case of juvenile recurrent respiratory papillomatosis

I. Navales$^{a, b}$, P. Paredes$^a$, M. Cols$^b$, A. Perissinotti$^a$, M. Vancells$^c$, F. Pons$^{a, d}$

$^a$ Servicio de Medicina Nuclear, Hospital Clinic, Barcelona, Spain
$^b$ Servicio de Pediatría, Hospital Sant Joan de Déu, Universidad de Barcelona, Barcelona, Spain
$^c$ Servicio de Cirugía Pediátrica, Hospital Sant Joan de Déu, Universidad de Barcelona, Barcelona, Spain
$^d$ Servicio de Medicina Nuclear, Hospital Clinic, Universidad de Barcelona, Barcelona, Spain

A B S T R A C T

Juvenile recurrent respiratory papillomatosis (JRP) is an infectious disease caused by the growth of papillomas in the airway. Up to 4% of these cases degenerate into squamous cell carcinoma. We present the case of a 17-year-old female patient with JRP in which the utility of $^{18}$F-FDG-PET/CT in the characterization of suspicious papillomatous lesions of malignancy is evaluated. Morphometabolic techniques, CT scan and PET/CT scans were suggestive of malignancy. However, this was not confirmed in the histopathological analysis after its resection.

The $^{18}$F-FDG-PET/CT does not seem to be a useful tool for early detection of malignancy in JRP. However, it does increase the diagnostic accuracy of the biopsy as it identifies the most active lesions and, therefore, those most likely to be malignant.

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Utilidad de la tomografía por emisión de positrones con $^{18}$F-FDG en un caso de papilomatosis pulmonar recurrente juvenil

R E S U M E N

La papilomatosis pulmonar recurrente juvenil (PPRJ) es una enfermedad infecciosa que provoca el crecimiento de papilomas en la vía respiratoria en la que hasta en un 4% de los casos degeneran hacia un carcinoma de células escamosas. Presentamos el caso de una paciente de 17 años con PPRJ en la que se valoró la utilidad de la $^{18}$F-FDG-PET/CT ante la sospecha de malignización de las lesiones papilomatosas. Las técnicas de imagen morfometabólicas, la TC y la PET/TC fueron sugestivas de malignidad. Sin embargo, esta no fue confirmada en el análisis anatomo-patológico tras su resección.

La F-DG-PET/TC no parece una herramienta útil para la detección precoz de malignidad en la PPRJ, aunque sí aumenta la rentabilidad diagnóstica de la biopsia al identificar las lesiones más activas y, por lo tanto, con mayor posibilidad de ser malignas.

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Introduction

Recurrent pulmonary papillomatosis (RPP) is an infectious disease which produces the growth of papillomas in the respiratory tract. The most frequently involved organ is the larynx while pulmonary involvement only occurs in 1% of the patients. The etiology of RPP is infectious, being caused by the human papilloma virus (HPV). The juvenile variant of this disease (RJP) affects children under the age of 12 years, is more severe than the adult variant and is associated with vertical perinatal transmission.

The incidence in subjects under the age of 14 years is of 4.3 cases/100,000 inhabitants. Treatment is based on resection of the accessible lesions and the use of antivirals and immunomodulators with the objective of slowing the evolution of the disease since curative treatment is not currently available. Periodical resection of the lesions carries a high morbidity, with more than 4 surgical procedures per year, and the need for tracheotomy in children of less than 2 years of age is not infrequent.

In up to 4% of the cases malignant degeneration of the papillomatous lesions is produced, leading to squamous cell carcinoma, generally in the lesions of the pulmonary or bronchial parenchyma.

This evolution to malignancy is associated with the HPV-6 and HPV-11 subtypes, with the latter also presenting greater disease severity. In this context, morphometabolic imaging tests are useful in the follow up of the disease and in the detection of malignancy.

We present the case of a patient with RJP in whom the utility of $^{18}$F-FDG-PET/CT on suspicion of malignancy of the papillomatous lesions was evaluated.

Clinical case

A 17-year-old patient had been diagnosed with RJPP by HPV-11 infection in the first months of life with no other pathological history of interest. During the course of the disease the patient...
had undergone periodical surgical interventions for resection of the papillomatous lesions.

In an intravenous enhanced contrast lung CT scan performed in a control consultation, consolidation of the airway space was observed from the basal pyramid to the right hilar region compatible with an inflammatory process of slow evolution. This image had progressed with respect to previous studies. In the left lung a second mass was visualized in the posterior basal segment with a hypodense, necrotic zone which could not be definitively determined as an adenopathy or pulmonary nodule. Despite the first lesions of the inferior right lobe (IRL) having appeared 10 years previously, these had currently progressed and had the potential of developing a squamous carcinoma. The patient was referred to the Department of Nuclear Medicine for assessment of metabolic behavior and to corroborate the suspicion of malignancy. A PET/CT scan was performed, showing pathologic uptake of the pulmonary lesion of the IRL with a component of distal atelectasis with no uptake of $^{18}$F-FDG. The left pulmonary lesion presented a hypermetabolic behavior. A third increased uptake was found in the right hilum (Fig. 1). These lesions were interpreted as suggestive of malignancy due to their hypermetabolism.

In view of these findings resection of the mass localized in the IRL was performed by thoracoscopy since this lesion fulfilled the criteria of malignancy in both the CT study as well as the PET/CT. The anatomopathological study of the lesion demonstrated bronchial and alveolar involvement by papillomatosis. The bronchial tissue sample showed an inflammatory infiltrate with abundant invasive endobronchial papillomas presenting squamous metaplasia while the pulmonary parenchyma showed a fibrohemorrhagic infiltrate. The proliferative index (Ki67 cellular marker) of the basal bronchial layer was elevated. Five months later a control of disease evolution was carried out with $^{18}$F-FDG-PET/CT which demonstrated the persistence of the right pulmonary mass which was interpreted as recurrence. The left mass demonstrated morphometabolic improvement compared with the previous study (Fig. 2). Despite the reduction in the grade of uptake of the lesion in the IRL, the persistence of significant hypermetabolism led to a new surgery involving segmentectomy of the affected zone of the IRL, with the resection of the pleural adherences, achieving good re-expansion of the remaining tissue. The histologic results did not show cancer cells.

**Discussion**

We have presented a case of RJPP in a 17-year-old patient who underwent 2 $^{18}$F-FDG-PET/CT studies for suspicion of malignancy of the papillomatous lesions. Both studies demonstrated elevated uptake of the pulmonary lesions suspicious of malignancy.
Anatomopathologic analysis of both the surgical pieces as well as the posterior segmentectomy did not show evidence of cancer but did demonstrate squamous metaplasia and an elevated proliferative index, representing a false positive result of the $^{18}$F-FDG-PET/CT.

Similar to what has previously been described, $^7,^8$ the avidity of the $^{18}$F-FDG in our patient is justified by the elevated cellular proliferation and correlates with the aggressiveness of these lesions. Other similar cases in the literature have been found suggesting that $^{18}$F-FDG-PET/CT is not useful in the early detection of malignancy. The histology findings of our patient did not demonstrate malignancy but did show indirect signs of possible malignancy such as an elevated proliferative index (Ki67). A good correlation between the grade of FDG uptake and the increase in the Ki67 index has been associated with other pulmonary neoplasms.$^9,^{10}$ It is reasonable to think that large papillomatous lesions which present a negative $^{18}$F-FDG-PET/CT study will not demonstrate an elevated proliferative index (Ki67) or aggressive behavior and will less likely be malignant. Nonetheless, further studies contributing better knowledge of the metabolic characteristics of these lesions are necessary to generalize this affirmation in this infrequent disease.

The patient presented several morphological lesions in both pulmonary bases, at different bronchial levels and in the right hilum. The PET/CT was useful to guide the biopsy since it identified the active lesions and thus, those with a greater possibility of malignancy, increasing its diagnostic profitability.

The $^{18}$F-FDG-PET/CT does not seem to be a useful tool for the early detection of malignancy in RJPP, although it does have a role in the identification of lesions presenting greater aggressiveness and therefore, having a greater probability of malignancy, being a guide for performing biopsies.

References