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Original Article

Can positron emission tomography support the characterization of immune-mediated inner ear disease?☆

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ABSTRACT

Introduction: To evaluate the utility of positron emission tomography-computed tomography (PET/CT) as an imaging tool for the characterization of immune-mediated inner ear disease (IMIED), providing measurements of the inner ear region activity as well as detecting possible involvement of other organs.
Material and methods: The study included 28 patients with IMIED and 4 sex-matched and age-matched control subjects with no history of ear disease.
Eighteen patients were considered to be suffering from primary IMIED and 10 patients from secondary. PET/CT scans with ^{18}F-FDG were performed to assess systemic involvement as well as inner ear region activity.

Interpretation of PET/CT scans was performed independently by two nuclear medicine physicians blinded to clinical history. In order to assess inter-rater agreement before performing the analysis of the inner ear, different Bland & Altman plots and the intraclass correlation coefficients were estimated.
Results: Different metabolically active foci findings were reported in 13 patients. Four patients diagnosed as primary IMIED showed thyroid and aorta activity. Regarding the inner-ear semiquantitative analysis, the inter-rater agreement was not sufficiently high. Comparisons between groups, performed using Mann–Whitney test or Kruskal–Wallis tests, showed no differences.
Conclusions: The study showed ^{18}F-FDG PET/CT could be an important tool in the evaluation of IMIED as it can support the characterization of this entity providing the diagnosis of unknown or underestimated secondary IMIED. Nevertheless, we consider PET is not an adequate tool to approach the inner ear because of the small size and volume of the cochlea which makes the assessment very difficult.

¿Puede la tomografía por emisión de positrones ayudar en la caracterización de la enfermedad inmunomediada del oído interno?

Keywords:
Immune-mediated hearing loss
Positron emission tomography
Inner ear
Systemic autoimmune disease
FDG

RESUMEN

Introducción: Evaluar la utilidad de la PET/TC con ^{18}F-FDG en la caracterización de la enfermedad inmunomediada del oído interno primaria (EIOI) aportando datos que ayuden a valorar la actividad inflamatoria y la existencia o ausencia de enfermedad sistémica asociada.
Material y métodos: Estudio prospectivo sobre 28 pacientes con sospecha de EIOI o EIOI primaria diagnosticada y controles sin enfermedad ótica conocida con PET FDG realizado por otro motivo.
Dieciocho pacientes presentaban EIOI primaria y diez EIOI secundaria. A todos se les realizó un PET/TC con ^{18}F-FDG para valorar la actividad metabólica en el oído interno y la presencia de afectación sistémica.

La interpretación del resultado del PET fue realizada por dos médicos nucleares sin conocimiento de la clínica del paciente. Para valorar la reproductibilidad de las medidas se realizaron análisis Bland&Altman y correlación de coeficientes interclase.
Resultados: Se encontraron hallazgos sospechosos de afectación sistémica en 13 pacientes. Cuatro de ellos correspondieron a pacientes diagnosticados previamente de EIOI primaria que mostraron actividad inflamatoria (tiroidea y aórtica). En cuanto al análisis semicuantitativo de la actividad metabólica en el oído interno, la variabilidad interobservador fue muy alta y no fue posible establecer diferencias adecuadas entre grupos.

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Conclusiones: Este estudio demuestra que el PET-TC con 18F-FDG puede tener un papel en la evaluación de pacientes con sospecha de EIOI primaria descartando la presencia de datos que sugieran inflamación sistémica. Consideramos que no es adecuado tratar de cuantificar la actividad metabólica del oído interno probablemente por el pequeño tamaño del mismo.

Introduction

Immune-mediated inner ear disease (IMIED) is an accepted clinical syndrome presenting as rapidly progressive sensorineural hearing loss which responds to steroids.[1] Initially, it may present as a sudden unilateral disease, often progressing to bilateral deafness or sensorineural hearing loss, occasionally associated with vestibular symptoms. Idiopathic sudden sensorineural hearing loss (sudden deafness) and Meniere's disease can share the clinical picture and mimic IMIED. Some forms of both entities are thought to be due to an autoimmune process[2,3] (Table 1).

The syndrome refers to a pathology restricted to the ear (primary IMIED) or to multisystemic, organ-nonspecific autoimmune diseases involving the inner ear (secondary IMIED).[4] Primary IMIED is a rare disorder and it represents a challenge for otologists because of the lack of a definitive diagnostic test.[5]

Since IMIED is one of the few inner ear disorders reversible to medical therapy, many attempts have been made in order to improve early diagnosis, mainly in primary forms. Thus, high risk profile[6] and MRI studies in patients affected by sudden sensorineural hearing loss have been suggested.[7]

Positron emission tomography (PET/CT) has become an excellent tool to assess disease activity and prognosis in some systemic autoimmune diseases like systemic lupus erythematosus (SLE). By targeting the increased glucose uptake of infiltrating granulocytes, tissue macrophages and activated lymphocytes, positron emission tomography with fluorine-18 fluorodeoxyglucose (^{18}F-FDG PET/CT) has been shown to visualize large concentrations of these cells in lymphoid organs where antigen presentation and lymphocyte activation occur.[8] Because of its good performance in the field of inflammatory disease, PET/CT has been introduced as a diagnostic tool in the algorithms of different multisystemic inflammatory processes.[9]

A pilot study reported that FDG can be used in PET to assess disease activity in patients with IMIED.[10]

The aim of the present study is to validate the role of PET/CT in the characterization of primary and secondary IMIED, providing measurements of the inner ear region activity as well as possible involvement of other organs. This analysis could be remarkable in primary IMIED patients, who show negative serological tests, making difficult an early diagnosis and prompt treatment.

Material and methods

Twenty eight patients affected by IMIED, 20 women and 8 men (mean age 43.7 years; range 15–72 years) assisted in the Department of Otorhinolaryngology from January 2013 to November 2016, have been included in the study. Four sex-matched and age-matched without any history of autoimmune inner ear disease or active inflammatory disease or cancer (referred for neurological PET) were considered as control subjects. Exclusion criteria: neoplasm, active infections, vasculitis, or active inflammatory processes in the temporal bone region. There were only four control patients included due the difficulty to obtain patients that fulfilled the criteria and had the adequate age of the patients in the study.

Eighteen patients were considered as primary IMIED and 10 patients were included in the secondary IMIED group (Table 2). Informed consent was obtained from all patients and controls. The study was approved by the Clinical Research and Ethics Committee of our institution (PI 15/16, Acta 04.16). Patients were studied according to our diagnostic protocol (Fig. 1) designed for this study. Most patients had been treated with high-dose corticosteroid therapy (methylprednisolone or prednisolone, 1 mg/kg/day, intratympanic methylprednisolone and methotrexate, 10.0–20.0 mg/week) before PET scanning. None had hyperglycemia or diabetes.

PET/CT images were obtained using a dedicated PET/CT system (Biograph 6, Siemens Medical Systems, Knoxville, TN, USA). Patients were requested to fast for 6 h before the study. Acquisition

Table 1
Clinical manifestations of IMIED. Sensorineural hearing loss (SNHL) is responsive to corticosteroids.

Asymmetric bilateral rapidly progressive SNHL (weeks or months).
Bilateral sudden SNHL (hours to days).
Recurrent sudden SNHL (more than 2 episodes in one year).
Fluctuating SNHL in one ear following inner ear damage in the opposite ear (CMV infection, inner or middle ear surgery, sudden SNHL) (days to years after the event).
Bilateral Meniere's disease.

Table 2
Systemic autoimmune diseases in secondary IMIED patients included.

Disease	*N*
Antiphospholipid syndrome	1
Antiphospholipid syndrome + Sjogren syndrome	1
Sjogren syndrome	1
Autoimmune thyroiditis	5
Autoimmune thyroiditis + autoimmune encephalitis	1
Connective disease + celiac disease	1

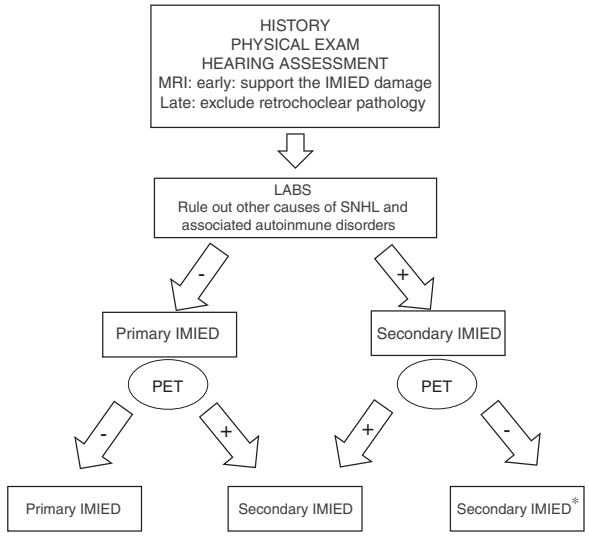

Fig. 1. Stepwise algorithm for the approach to a patient with suspected IMIED. *Negative PET in Secondary IMIED may be due to inactive disease and/or immunosuppressive therapy.