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Original Article

^{99m}Tc-HMPAO brain SPECT in the monitoring of cerebral vasculitis therapy[☆]

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ABSTRACT

Objective: The central nervous system (CNS) may be involved in a variety of inflammatory diseases of the blood vessels, generally known as vasculitis. The clinical diagnosis of such involvement in early stages is difficult, since a mild cognitive impairment can be the only symptom. It was hypothesized that brain-perfusion SPECT would be able to reveal CNS involvement and to monitor the course of the disease. The purpose of this study was assess if and when an improvement of cerebral perfusion can be registered by SPECT during the follow-up of these diseases.

Material and methods: Eighteen patients affected by Systemic Lupus Erythematosus (SLE), 22 by undifferentiated vasculitis (UV), 5 by Behcet's disease (BD) and 5 by primary Sjogren's Syndrome (pSS) were enrolled in this prospective study. A ^{99m}Tc-HMPAO brain perfusion SPECT was performed before the treatment and was repeated during the follow-up at different time intervals. Image analysis was performed on 10 cerebral areas using a specific software.

Results: In the SLE patients, no significant improvement of brain perfusion was found. On the contrary, in the UV the cerebral uptake of the tracer significantly improved from the twenty-fourth month (18/22 patients). Patients with BD showed an improvement of scintigraphic findings (5/5 patients), while a similar result was obtained only in 2 of the patients with pSS.

Conclusions: In conclusion, brain SPECT seems to be able to monitor the disease in UV, indicating the moment when an improvement of the cerebral perfusion is achieved. In SLE patients this scintigraphic technique did not show a significant improvement in CNS perfusion.

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^{99m}Tc-HMPAO SPECT cerebral en la monitorización de la terapia de vasculitis

RESUMEN

Objetivo: El sistema nervioso central (SNC) puede estar afectado en una variedad de enfermedades inflamatorias de los vasos sanguíneos, generalmente conocidas como vasculitis. El diagnóstico clínico de dicha afectación en etapas tempranas es difícil, ya que un leve deterioro cognitivo puede ser el único síntoma. Se planteó la hipótesis de que la SPECT de perfusion cerebral podría mostrar la afectación del SNC y podría servir para controlar el curso de la enfermedad. El propósito de este estudio fue evaluar si y cuándo una mejora de la perfusión cerebral puede ser registrada por SPECT durante el seguimiento de estas enfermedades.

Material y métodos: Dieciocho pacientes afectados por Lupus eritematoso sistémico (LES), 22 por vasculitis indiferenciada (UV), 5 por la enfermedad de Behcet (BD) y 5 por el síndrome de Sjogren Primario (pSS) se incluyeron en este estudio prospectivo. Se realizó una SPECT de perfusión cerebral con ^{99m}Tc-HMPAO antes del tratamiento, y se repitió durante el seguimiento a diferentes intervalos de tiempo. El análisis de imagen se realizó en 10 áreas cerebrales utilizando un software específico.

Resultados: En los pacientes con LES no se encontró una mejora significativa de la perfusión cerebral. Por el contrario, en la UV la captación cerebral del trazador comenzó a mejorar significativamente desde el vigésimo cuarto mes (18/22 pacientes). Los pacientes con BD mostraron una mejora de los hallazgos gammagráficos (5/5 pacientes), mientras que sólo se obtuvo un resultado similar en dos de los pacientes con pSS.

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Conclusiones: En conclusión, el SPECT cerebral parece ser capaz de monitorizar la enfermedad en UV, evaluando cuándo se puede registrar una mejoría de la perfusión cerebral. En los pacientes con LES, esta técnica gammagráfica no ha encontrado una mejoría significativa en la perfusión del SNC.

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Introduction

The central nervous system (CNS) may be involved in a variety of inflammatory diseases of the blood vessels, generally known as vasculitis.

Vasculitis is defined as an inflammation of the blood vessels with or without necrosis of the vessel wall. They are classified into primary and secondary subtypes: the primary vasculitis of the central nervous system is a rare disorder of unknown aetiology specifically targeting the CNS small vessels, whereas in the secondary subtype the systemic vasculitis involves the CNS among other organs and systems. The majority of CNS vasculitis are secondary forms. A further classification is based on the etiopathogenesis and it includes immuno-allergic, infectious and neoplastic forms. In each of these forms, to confirm the diagnosis of vessel inflammation, histological examination is usually required.¹

Due to the low incidence of these pathologies, there is a lack of epidemiological studies and valid data about the frequency of CNS involvement in each type of autoimmune vasculitis. Approximately, in Systemic Lupus Erythematosus (SLE) cerebral involvement affects nearly 40% of patients, but it seems to be directly related to vasculitis in less than 10% of these cases only. It has been reported in around 5% of cases in primary Sjogren's Syndrome (pSS) and in 10–30% of patients diagnosed with mixed connective tissue diseases. The frequency of neuro-Behçet is around 5–10%.²

In general, the clinical diagnosis of CNS vasculitis is difficult, particularly in early stages, in which a mild cognitive impairment can be the only symptom.³ Furthermore CNS involvement can precede clinical diagnosis by many years and determine an underestimation of other neurological and/or systemic diseases.⁴ Nevertheless, a prompt diagnosis and treatment of these pathologies can improve the clinical manifestations and the prognosis of the patients.

To date, there is no single diagnostic test that is sensitive and specific for neuropsychiatric manifestations related to vasculitis. The assessment of individual patients is based on clinical neurologic and rheumatologic evaluation, immune-serologic testing, brain imaging, and psychiatric and neuropsychological assessment. These examinations are used to support or refute the clinical diagnostic impression and to exclude alternative better explanations.⁵

The most used imaging techniques, such as magnetic resonance imaging (MRI), have shown to be insufficiently sensitive and specific in revealing the cerebral damage related to vasculitis, while the brain perfusion – Single Photon Emission Computed Tomography (BP-SPECT) seems to provide better results.^{6,7} Furthermore, it has been hypothesized that BP-SPECT could be able to monitor the course of the disease and the treatment, allowing to distinguish between patients with high likelihood of obtaining benefit from a specific treatment, and non-responders, to whom unnecessary side effects can be avoided.⁸ Such a distinction would be of paramount importance if you know how soon after initiating treatment you are entitled to regard a patient as responders.

The aims of this study was to monitor the treatment of cerebral vasculitis in order to assess if and especially when, during the course of the disease, an improvement of cerebral perfusion can be registered and if there is a correlation between cerebral perfusion and non-focal CNS involvement in autoimmune diseases both in the diagnostic and in the follow up stage.

Material and methods

Patients

Fifty patients (47 females and 3 males, mean age 39.8 years \pm 4.2) affected by autoimmune systemic vasculitis previously diagnosed according to American College of Rheumatology (ACR) criteria, underwent to our observation from 2010 to 2015 and were consecutively enrolled in this prospective study. All patients complained non-specific clinical symptoms of CNS involvement.

Based on diagnosis, this group of patients can be subdivided in 18 patients suffering by SLE, 22 by undifferentiated vasculitis (UV), 5 by Behcet's disease (BD) and 5 by pSS.

Inclusion criteria were: 1) age less than 45 years; 2) negative basal brain MRI; 3) presence of non-focal neurological signs and neuropsychiatric symptoms; 4) no corticosteroids treatments for at least 3 months prior to basal BP-SPECT, 5) time from diagnosis to basal BP-SPET less than 2 years.

Cardiovascular risk factors including hypertension, diabetes, dyslipidemia, cardiological illnesses, arrhythmias and cigarette smoking were considered as exclusion criteria, as well as acute and chronic infectious diseases, the presence of familiar and personal history of other neurological and psychiatric disorders or of neoplasms.

Written informed consent was obtained from all patients and the study protocol was approved by our Institutional Ethics Committee and conducted in accordance with the Ethical Guidelines of the 1975 Helsinki Declaration.

Clinical evaluation

All patients underwent a wide neurologic anamnestic investigation, objective examination and a panel of serological tests. Specific subjective symptoms were evaluated with appropriate tools.

The Second Edition of the International Classification of Headache Disorders (ICHD-II) was applied to establish a headache diagnosis and score. The psychiatric assessment was based on history and clinical interview focused on: 1) current or past psychopathological disorders; 2) structure of the personality; 3) signs and symptoms of reactive disorders to chronic illness, steroids, or disease-modifying (biological) therapies.

All patients underwent a global screening test with Clinical Global Impression Severity Scale (CGIs) and the following specific tests to detect possible behavioural correlates of executive functions: Beck Depression Scale II – BDII, State–Trait Anxiety Inventory Y1 and Y2 – STAY.

Basal cognitive evaluation was based on Mini-Mental State Examination (MMSE) for cognitive efficiency and Brief Intelligence Test (TIB) for IQ. Regardless of screening tests, all patients underwent a complete neuropsychological assessment in order to explore the main cognitive domains by means of: Verbal Span; Trail Making Test (parts A & B); Rey Auditory Verbal Learning Test; The Rey-Osterrieth Complex Figure Test (ROCF) (with immediate and delayed recall); Test of Weights and Measures Estimation (STEP); Test of Phonological Verbal Fluency/Semantics; Corsi Block Tapping Test; Tower of London – Italian version; Token Test; Aachener-Aphasie Test. Raw scores were adjusted for age, sex, education parameters and where applicable, test-specific correction factors.

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