General Hospital Psychiatry 37 (2015) 134–138

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: http://www.ghpjournal.com

Homogeneous magnetic resonance imaging of brain abnormalities in bipolar spectrum disorders comorbid with Wilson's disease

Mauro Giovanni Carta, M.D. [a,*], Luca Saba, M.D. [b], Maria Francesca Moro, M.D. [a], Enrico Demelia, M.D. [b], Orazio Sorbello, M.D. [c], Mirra Pintus, (Licensed Psychologist) [a], Elisa Pintus, (Licensed Psychologist) [a], Tatevik Simavorian, (Undergraduate Researcher) [d], Hagop Akiskal, M.D., Ph.D. [d], Luigi Demelia, M.D. [c]

[a] Department of Public Health and Clinical and Molecular Medicine University of Cagliari, Italy, Cagliari, Italy
[b] Department of Radiology, Azienda Ospedaliero Universitaria (A.O.U.), di Cagliari-Polo di Monserrato s.s. 554 Monserrato, Cagliari, 09045, Italy
[c] UOC of Gastroenterology, Azienda Ospedaliero - Universitaria, Cagliari, Italy
[d] International Mood Center, University of CA, San Diego, USA

ARTICLE INFO

Article history:
Received 13 September 2014
Revised 17 January 2015
Accepted 19 January 2015

Keywords:
Wilson's disease
Bipolar spectrum disorders
Brain imaging
Basal ganglia
White matter

ABSTRACT

Background: The purpose was to determine if brain damage in Wilson's disease (WD) is different in comorbid bipolar spectrum disorders (BDs), comorbid major depressive disorder (MDD) or without any mood disorders.
Methods: An observational study was conducted on consecutive patients from a center for WD care. The study sample was divided by psychiatric assessment into WD without any mood disorders, WD with BDs and WD with MDD negative at Mood Disorder Questionnaire (MDQ).
Results: Thirty-eight WD patients were recruited (53.2% females): 21 without mood disorders (55.2%), 9 with comorbid BDs (26.7%) and 8 with MDD without MDQ+ (21.1%). The BDs showed a higher frequency of brain damage, reaching statistically significant differences in the basal ganglia ($P<.001$), in the overall brain ($P<.003$) and at the limit in the white matter ($P<.05$).
Conclusions: In WD, comorbidity with BDs is associated with earlier evidence of brain damage, especially in the basal ganglia. The results confirm the importance of screening and early diagnosis of BDs in WD. Future follow-up studies on large samples are required to confirm if detection of BDs may be an early marker of brain damage and if a good therapeutic response in BDs may improve the prognosis of WD.
© 2015 Elsevier Inc. All rights reserved.

1. Introduction

Wilson's disease (WD) is a rare inherited autosomal recessive disease in which copper accumulates in tissues. WD has a prevalence of around 1:30,000 [1]. The manifestations of WD depend on a gradual toxic accumulation of free copper which impairs organs such as the liver, brain and eyes [2]. Brain damage can arise very early, and it has been found using brain mapping techniques in the superior frontal (Brodmann area 6), prefrontal (Area 9), parietal (Area 40) and occipital (Areas 18 and 39) cortices in temporal gyri (Areas 37 and 21), in caudatus and in putamen [3]. Early magnetic susceptibility was also found in substantia nigra, red nucleus and pallidum of WD patients [4].

Psychiatric manifestations have been reported after Wilson's original description of such a disease. He found psychiatric symptoms in two thirds of his patients, beginning with the traditional interpretation of schizophrenia-like psychosis as typical manifestation of WD [5]. Today, it is known that a high frequency of a large spectrum of psychiatric symptoms characterizes WD, although a specific association between bipolar spectrum disorders (BDs) and WD was recently found [6]. Patients with WD comorbid with BDs are also characterized by a worsening quality of life compared with those without BDs and even those with major depressive disorder (MDD) [7].

Some, but not all, of the brain areas affected by damage typical of WD were also found to be injured in patients with BDs without WD. In fact, among the structural alterations in BD patients, the most frequently reported was at the level of frontal, temporal and insular cortices and amygdala; ventriculomegaly was found as well [8]. Basal ganglia abnormalities such as a decrease in volume have also been reported [9].

The purpose of this work is to verify in a sample of patients with WD if brain damages are different from those with comorbid BDs compared to those with comorbid MDD or those with no mood disorders. We will also seek to highlight differences with respect to disease duration.

2. Methods

2.1. Study design

This was a controlled observational study. On the basis of psychiatric assessment, the study sample was divided into patients with WD without

* Corresponding author.
E-mail addresses: mgcarta@tiscali.it (M.G. Carta), lucasaba@tiscali.it (L. Saba), mfmoro@gmail.com (M.F. Moro), ldemelia@pacs.unica.it (E. Demelia), ldemelia@pacs.unica.it (O. Sorbello), mirra.pintus@hotmail.it (M. Pintus), pintuselisa@yahoo.it (E. Pintus), tsimavorian@gmail.com (T. Simavorian), hakiskal@ucsd.edu (H. Akiskal), ldemelia@pacs.unica.it (L. Demelia).

http://dx.doi.org/10.1016/j.genhosppsych.2015.01.006
0163-8343/© 2015 Elsevier Inc. All rights reserved.

any mood disorders, WD patients with BPs, and patients with WD and comorbid MDD negative at screening for bipolar spectrum disorders.

2.2. Patients

The subjects were consecutive WD patients seen between January 2010 and September 2013 at the Gastroenterology Unit of the University Hospital in Cagliari, Italy. Basic demographic data were extracted from routine medical records.

2.3. Psychiatric assessment

The psychiatric interviews were carried out using two validated tools. To assess the presence of *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) psychiatric disorders, the Advanced Neuropsychiatric Tools and Assessment Schedule (ANTAS) [10,11] was adopted. ANTAS is a semistructured clinical interview partially derived from the Structured Clinical Interview for DSM-IV-TR Axis I Disorder (SCID for DSM-IV) [12]. ANTAS was administered by physicians or psychologists with experience in psychiatric clinic and research. The reliability of diagnostics of mood and anxiety diagnoses using ANTAS vs. SCID was previously measured and published: the mean *K* was 0.85 [11]. For detected subthreshold manic symptoms and bipolar spectrum disorders, the Mood Disorder Questionnaire (MDQ, Italian version) [13] was used. The cutoff of MDQ adopted was 7 (bipolar cases identified by a score of 7 or more) [13].

We adopted a broad concept of BDs [14] so that the group of BDs would include WD patients positive at MDQ and/or BD patients detected with ANTAS coherently (with diagnosis of DSM-IV bipolar I or bipolar II disorder). The group of MDD would include MDD detected by ANTAS but exclude patients with MDD positive at the screening for BDs (classed in BDs).

2.4. Gastroenterology assessment

Diagnosis of WD was made if the patient had hepatic (jaundice, hepatomegaly/splenomegaly, ascites/edema, variceal hemorrhage) and/or neurologic signs of disease (dysarthria, dysphagia, apraxia and a tremor–rigidity syndrome) in addition to at least two of the following criteria (adapted and modified from Ref. [15]): (a) positive family history of WD; (b) low ceruloplasmin level (<20 mg%); (c) presence of Kayser–Fleischer ring by slit lamp (examination with a slit lamp); (d) liver biopsy suggestive of WD [positive staining of copper-associated protein (rhodanine or orcein stain), presence of glycogenated nuclei, micro- or macrovescicular steatosis or ultrastructural changes defined by electron microscopy] as measurement of liver copper content (of >250 μg/g dry weight); (e) elevated baseline 24-h urinary copper excretion (more than 100 μg/24 h or more than1600 μg/24 h after D-Penicillamine challenge test).

The patients with indeterminate results required additional testing, such as molecular testing for ATP7B mutations, using polymorphic markers of the promoter of the gene ATP7B, the most frequent mutation in Sardinia: 5'UTR of −441/−427, promoter region [16].

The following tests of liver function were conducted in cases of suspected diagnosis: alanine aminotransferase (nv <41 UI/L), Gamma-glutamyl transpeptidase (nv <61 IU/L), alkaline phosphatase (nv <270 IU/L), total bilirubin (nv <1.0 mg/dl), indirect bilirubin (nv <0.80 mg/dl) and other routine laboratory data (including viral markers and autoantibodies) were measured using standard methods to evaluate the degree of liver affection as well as to identify/exclude any associated hepatic condition[17].

All our patients were tested for copper metabolism parameters: quantitative serum ceruloplasmin concentration performed using automated clinical chemistry analyzers (Array Protein System 360; Beckman Instruments, Brea, CA, USA) using a nephelometric assay (reference range between 200 and 600 mg/L); serum non-ceruloplasmin-bound copper concentration; serum copper concentration and 24-h urinary copper excretion, measured using an inductively coupled optical emission spectrometer (reference range for serum copper 10–22 μmol/L, urinary copper output >1.5 μmol/24 h).

Histological evaluation: In patients who consented to the histological study, liver biopsies were obtained with the Menghini technique under ultrasound guidance. For histological examination, paraffin-embedded 4-mm sections were stained with hematoxylin and eosin, rhodanine and natural orcein. The liver histology was evaluated in a blinded manner according to the classification of Desmet using grading and staging scores.

Hepatic parenchymal copper concentration (>250 micrograms/g dry tissue) was also detected after hepatic agobiopsy. The determination of metal content in tissue was performed by atomic absorption spectrometry (Instrumentation Laboratory Video 22) (reference range <250 micrograms/g dry tissue).

2.5. Brain magnetic resonance imaging (MRI) technique

Imaging examinations were performed using a 1.5-T superconducting magnet (Philips, Best, the Netherlands) with a head coil according to a standardized protocol. In each subject, the conventional diffusion weighted imaging (DWI) was performed with a single-shot spin-echo with two diffusion-sensitivity values of 0 and 1000 s/mm^2 along the transverse axis. As part of our general brain protocol, axial and sagittal two-dimensional fluid attenuated inversion recovery (FLAIR) images (10,000/140/2200 ms for repetition time/echo time (TR/TE); matrix: 512×512; field of view: 240×240mm2; section thickness: 5 mm) were acquired. In addition to FLAIR and DWI sequences, axial spin-echo T1-weighted images (500–600/15/2 for TR/TE/excitations) and fast spin-echo T2-weighted images (2200–3200/80–120/1,2 for TR/TE/excitations; turbo factor, 2) were also obtained with the same section thickness. Acquisition date and participant identification were removed from all images, and two experienced radiologists in consensus (blinded for peer review, with 11 and 6 years of experience, respectively), unaware of the clinical data, reviewed all patients for presence and severity of alteration in the basal ganglia mesencephalon and for presence and severity of atrophy. For the assessment of the alteration of the basal ganglia, the FLAIR acquisition was mainly used, and the following visual five-point grading scale was used: 1 (no alterations); 2 (focal lesions); 3 (early confluent lesions); 4 (diffuse involvement of one of the thalamus, pallidus, putamen and caudate) and 5 (diffuse involvement of two or more of the thalamus, globus pallidus, putamen and caudate). The midbrain involvement was also assessed using a five-

Table 1
Study sample

Sample	Number	Age	Sex (female)	Age at onset	Years with WD
Total sample	38	42.2±11.8	21 (53.2%)	28.2±17.3	14.0±5.5
With no mood disorder	21	41.3±13.0	11 (55%)	24.4±16.6	16.9±3.6
BDs (MDQ+ or SCID-DSM-IV)	9	42.4±12.1	3 (33.3%)	29.5±18.7	12.9±6.6
MDD without MDQ+	8	39.4±8.9	6 (75%)	23.3±16.9	16.1±8.0
Statistical comparisons between groups		*F*=0.137 *P*=.872 df 2, 35, 37 (one-way ANOVA)	Without vs. BPs *P*=.440 Without vs. MDD *P*=.408 MDD vs. BPs *P*=.153 (Fisher's Exact Test)	*F*=0.366 *P*=.696 df 2, 35, 37 (one-way ANOVA1)	*F*=1.688 *P*=.200 df 2, 35, 37 (one-way ANOVA)

Download English Version:

https://daneshyari.com/en/article/3237579

Download Persian Version:

https://daneshyari.com/article/3237579

Daneshyari.com