

Wilson Disease Watch

July-September 2012. vol 5

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EuroWilson: European **Wilson's Disease Network**
Improving information, knowledge and access to expertise and care



Transcranial sonography in Wilson's disease

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Summary

Transcranial sonography (TCS) has been recently recognized as a reliable and sensitive tool in detecting basal ganglia (BG) abnormalities in several movement disorders, where different patterned hyperechogenic lesions were demonstrated. The aim of this study was to investigate changes in TCS in a larger group of clinically stable patients with Wilson's disease (WD), and to correlate them with demographic and clinical data. TCS was conducted in 54 consecutive, clinically stable patients with WD who were classified as predominantly neurologic or hepatic form of the disease and were adequately assessable by TCS from both sides. TCS revealed significantly higher prevalence of SN ($p = 0.007$) and LN hyperechogenicity (0.001) in WD patients when compared to controls. Moderate to marked SN hyperechogenicity was found in 31.5% of WD patients (in 42% and 7% of those with neurologic and hepatic form of WD, respectively) and in 8% of healthy controls. Disease severity correlated with the hyperechogenicity of SN ($r = 0.303$; $p = 0.029$) and with the width of the third ventricle ($r = 0.351$; $p = 0.011$). There is only one report of TCS in WD previous to our study. Both studies proved the ability of TCS to detect accumulation of copper and probably other trace metals, such as iron and manganese, in the BG of WD patients.

Comments

We calculate that TCS is able to detect accumulation of copper and probably other trace metals, such as iron and manganese, in the BG of WD patients.

Take home message

TCS revealed significantly higher prevalence of SN and LN hyperechogenicity in WD patients when compared to controls. Disease severity correlated with the hyperechogenicity of SN and with the width of the third ventricle.



Analysis of clinical and biochemical spectrum of Wilson disease patients

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Summary

Background and Aims: Wilson disease (WD) is autosomal recessive disorder of copper metabolism. Wilson disease patients usually suffer from hepatic or neuropsychiatric complications. The symptoms appear between ages five to 35 but it can vary from two years to 72 years. **Materials and Methods:** Study was carried out from June 2008 to November 2010. This study included nine families with eleven cases of WD to determine clinical presentation, diagnostic findings (including laboratory results) and liver histology. It included 11 patients who presented with hepatic manifestations and/or Neuropsychiatric manifestations and/or family history suggesting features of WD. Patients with hepatitis B and C and those with history of taking antipsychotic drugs were excluded from the study. Patient's data was included in a well designed performa. Liver function test, serum ceruloplasmin, serum copper, 24 hour urinary copper, blood complete picture were analyzed. Quantitative data such as age, hemoglobin etc were expressed as mean with \pm SD and quantitative variables such as sex, movement disorders, hepatic involvement etc were expressed as frequency and percentage. **Results:** There were five male and six female patients with evidence of various manifestations here (i) hepatic in which they had only liver dysfunction (ii) hepatic and neurological (iii) neurological. The mean age of presentation was 8.7 ± 3.92 years (range 4–19 years) and 45% were male patients. Decreased serum ceruloplasmin, enhanced 24-h urinary copper excretion and signs of chronic liver damage were confirmed in all patients and Kayser–Fleischer rings (KF rings) in 72% of patients. In severe WD patients, serum prothrombin activity was less than 50%, serum ceruloplasmin were low and serum copper levels were high than those in non-severe WD patients. High degree of suspicion leads to early treatment with good outcome. **Conclusions:** The WD is rare but important cause of chronic liver disease. Clinical and biochemical analysis in cases of patients with unexplained liver disease with high degree of suspicion can lead to early treatment with good outcome.

Comments

This is first local study to elucidate the detailed clinical, biochemical analysis along with mutation analysis in ATP7B gene in Pakistani WND patients. Data related to Spectrum of ATP7B Gene Mutations in Pakistani Wilson Disease Patients: A Novel Mutation Is Associated with Severe Hepatic and Neurological Complication was published in Canadian international journal of biology vol. 2, No. 1 in January 2010.

Take home message

Such studies in Pakistan will help in screening carriers to prevent progression of disease in a family or population. Early diagnosis can lead to early treatment with good outcome.



Familial screening in Wilson's disease: Think at the previous generation!

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Article published in [J Hepatol](#). 2012 Jul 20 [Epub ahead of print]

Summary

Wilson's disease (WD) is an autosomal recessive disease caused by mutations in the ATP7B gene, resulting in accumulation of copper in various organs including liver, cornea, and brain. AADSL and EASL Guidelines have been published to help physicians in diagnosis and treatment.

We report diagnosis of WD in a 43-year-old asymptomatic father after his daughter had presented with a typical hepatic WD, and want to focus on recommendations about familial screening. The daughter (patient 1) was a previously healthy 10-year-old girl, who presented with hepatosplenomegaly. Additional testing confirmed the diagnosis of WD. Her parents were screened, although they were totally asymptomatic. The results obtained for the father (patient 2) were compatible with WD. By whole-gene sequencing, he was identified as a compound heterozygote and was treated with Zinc salts.

In case of WD, it is highly recommended to perform familial screening. Both Guidelines recommend screening first-degree relatives of the index case, suggesting siblings or children only. We usually know that WD occurs in siblings (25%) and the offspring (0.5%), but the risk also exists for the previous generation (0.5%), even if rarely reported. Moreover, WD disease occurs with different clinical presentations: hepatic, neurological, psychiatric disorder or asymptomatic. The phenotype of WD varies considerably among patients with the same genotype without any correlations, even within a single family. WD usually occurs between 3 and 40 years of age, but a later onset is possible.

Considering the possibility of late onset, absence of symptoms, and absence of phenotype-genotype correlation in WD, it seems necessary to screen the previous generation, especially the parents of a new patient, as illustrated in our case report. The modalities of familial screening are important too. In our family, standard genetic testing for parents (search only for the two index case's mutations) would not have been sufficient to diagnose WD in patient 2.

In conclusion, genetic counselling is essential for families of WD patients. Not only siblings and the offspring but also the previous generation of the index case must be screened by performing liver tests, explorations of copper metabolism, and suitable genetic testing.

Comments

Familial screening must include explorations of copper metabolism.

Take home message

Familial screening in Wilson Disease is essential not only for siblings and offspring but also for previous generation.



Teleconference on Long Term Follow Up Project

July 3rd, 2012

Summary kindly written by Dr Carla Lloyd from Birmingham Children's Hospital, UK

In attendance

Johann DEUTSCH, Austria

Mirjana KALAUZ, Croatia

Peter OTT, Denmark

Emeline RUANO, France

Roderick HOUWEN, The Netherlands

Karolina DZIEZYC, Poland

Piotr SOCHA, Poland

Marina MAGALHAES, Portugal

Andrea DEUTSCHMANN, Austria

Radan BRUHA, Czech Republic

Anne-Sophie BRUNET, France

Jean Marc TROCELLO, France

Anna CZLONKOWSKA, Poland

Tomasz LITWIN, Poland

Isabel GONCALVES COSTA, Portugal

Carla LLOYD, UK

Apologies

Pietro VAJRO, Italy (had tried to call in but number not working)

The objectives of this discussion were to check the progress of data collection and see whether there were any problems in obtaining long term follow up data.

Jean-Marc reported that there may be a problem in getting follow up data from Italy and he would ask Pietro if he could liaise with his colleagues in Italy to obtain the long term follow up data.

Each centre reported back:

All were happy with the forms and had not encountered many difficulties. Martin Fox entered many cases and there may be some problems in identifying these and obtaining follow up data.

Denmark asked if they could add more patients: Agreed to only provide long term follow up on patients registered in database.

A request was made that the forms be page numbered, patient id to be recorded on each page.

Word version to facilitate data recording. Centres can still choose to complete forms by hand and post, fax or scan to Emeline.

Piotr requested that INR and PT be recorded. Not all centres do INR so agreement reached that either PT or INR be recorded, with ULN. Results of PT or INR would be described as 'normal' or 'abnormal' as statistical analysis would be difficult using two different methods.

Hepatic assessment: capture information on fibroscan or other non invasive marker. Again not all centres performing fibroscan. Agreed liver function tests would be an indicator of hepatic function.

Neurological assessment: Could an evaluation scale be added to form. This would be difficult to analyse as data are not available for all patients.

Emeline agreed to modify the forms and send to centres as pdf and word versions.

Both Piotr and Carla reported that as they were following up paediatric patients who had moved to adult units the data collection may prove a little more challenging. Both agreed to obtain follow up data from adult centres where possible.

Jean-Marc confirmed that the Wilson Disease Centennial Symposium was being held in London on 5th and 6th October 2012 and that there would be a meeting for the EuroWilson group. Jean-Marc asked everyone to confirm with Emeline if they wished to attend the meeting. EuroWilson would fund everyone and Emeline will make all arrangements.



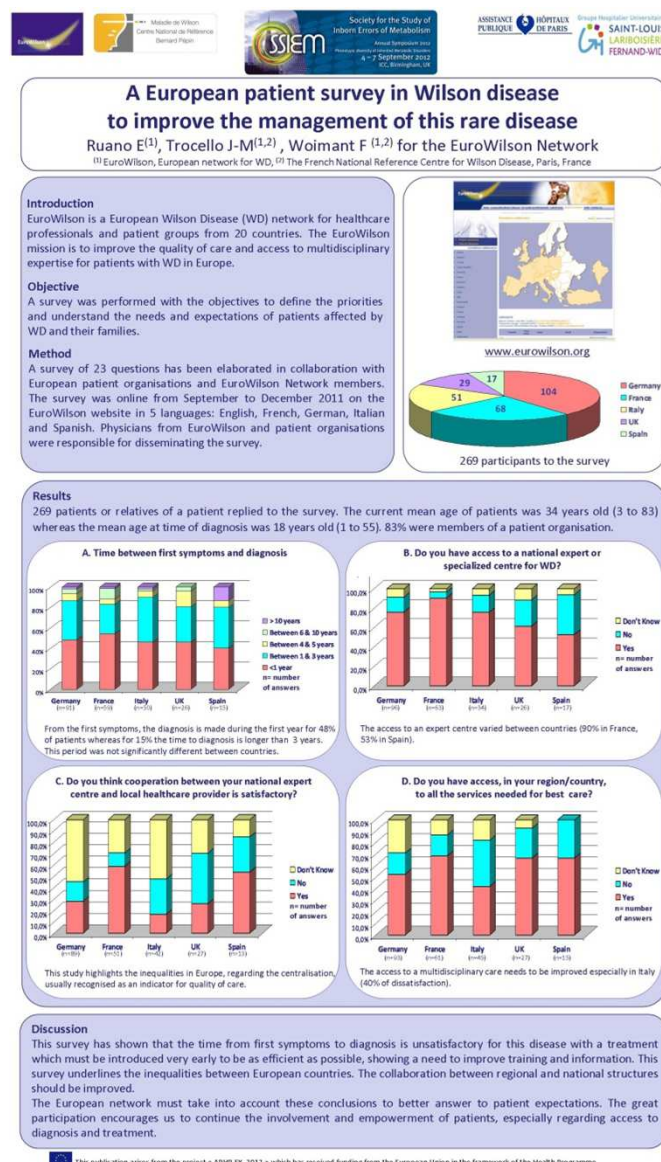
The Society for the Study of Inborn Errors of Metabolism Congress

September 6/7th, 2012
Birmingham, UK

Aims of the Society

The aim of the Society is to foster the study of inherited metabolic disorders and related topics. The Society, founded in 1963, exists to promote exchange of ideas between professional workers in different disciplines who are interested in inherited metabolic disease. Pursuing this aim by arranging scientific meetings, publications and in other ways considered appropriate by the Council.

EuroWilson presented a poster communication about the 2011 Patient Survey.



Agenda 2012

July

July 3rd,

*Follow Up Conference Call

July 5th,

*French Centre of Reference Meeting
Lyon, France

July 7th,

*Participation to the Annual Movement Disorder Society- European Section Summer School for young neurologists
*Presentation and case report of 2 Wilson Disease patients
Paris, France

September

September 6/7th,

*Poster communication in SSIEM Congress
Birmingham, UK

October

October 5/6th,

*Wilson's Disease Centennial Symposium
London, UK

October 8/9th,

*Oral presentation to the International Workshop Rare Diseases and Orphan drug registries
Rome, Italy

November

November 9th,

*Oral communication in ICNE Congress
Nice, France

