'CASSANDRA CURSE' OR A MODERN 'SISYPHUS BURDEN'? RECURRENT ATTACKS IN A COHORT OF BRAZILIAN PATIENTS WITH ACUTE HEPATIC PORPHYRIAS

Charles Marques Lourenço[1,2,4*], Lilian Sansão[2], Regina Albuquerque[2], Amadeu Jose Rodrigues Queiroz[2]; Maria da Penha[3], Eduardo Estephan[3], Maria da Penha Ananias Morita[1]; Erica Coelho[1] ; Jacqueline Harouche Rodrigues da Fonseca[4], Ieda Bussman[5]

[1] Neurogenetics Unit - Inborn Errors of Metabolism Clinics, Faculty of Medicine of São José do Rio Preto, São José do Rio Preto - São Paulo, Brazil
[2] National Reference Center for Rare Diseases, Hospital Materno Infantil - Faculty of Medicine of São José do Rio Preto, São José do Rio Preto - São Paulo, Brazil
[3] Serviço de Doenças Neuromusculares, Hospital de Base – FAMERP, São José do Rio Preto - São Paulo, Brazil
[4] Laboratório DLE, Grupo Fleury, Rio de Janeiro – RJ, Brazil
[5] BRAZILIAN PORPHYRIA ASSOCIATION – ABRAPO, Curitiba – Paraná, Brazil

Author's email: charles.lourenco@grupopardini.com.br

INTRODUCTION

Acute hepatic porphyrias (AHPs) include acute intermittent porphyria (AIP), hereditary coproporphyria (HCP) and variegate porphyria (VP), which result from autosomal dominant loss-of-function mutations in the third, sixth and seventh enzymes of the haem biosynthesis pathway, respectively.

The estimated prevalence of patients with AIP, VP and HCP is 5.9, 3.2 and <1 per million, respectively. Very few cases of severe homozygous dominant AHPs have been reported, with affected patients presenting with severe, infantile-onset symptomatology. The AHPs also include an autosomarecessive disorder, ALA dehydratase porphyria (ADP), with only 8 confirmed cases.

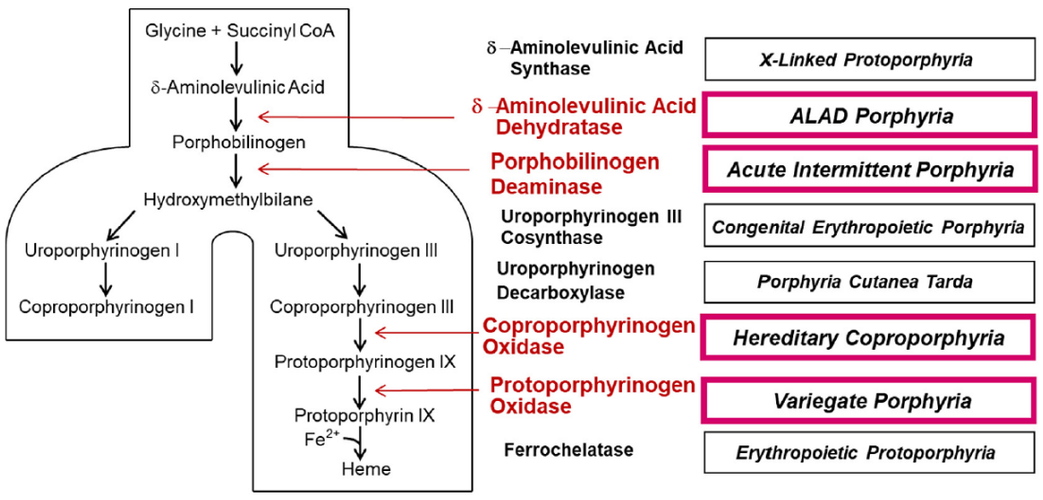

Figure 1 *Intermediates and enzymes of the heme biosynthetic pathway, the types of porphyria associated with altered activity of each enzyme. The four acute porphyrias are highlighted. Abbreviation: ALAD, δ-aminolevulinic acid dehydrataseUROD metabolic pathway (From Karl E. Anderson, Molecular Genetics and Metabolism, https://doi.org/10.1016/j.ymgme.2019.07.002)*

OBJECTIVES

To document the clinical features of Brazilian acute porphyria patients with recurrent crises and chronic symptoms and the impact on their quality of life.

METHODS

Retrospective data from patient records and clinical questionnaires/interviews with 24 patients with acute porphyrias followed in a reference center for porphyria treatment in Brazil. All cases had molecular confirmation and were diagnosed as part of the Alnylam Act initiative.

RESULTS

24 patients (20 females and four males) were enrolled. Media age of symptons onset was 22 years (range: 12–47 years). All patients reported recurrent porphyria related symptoms, such as pain, neurological and/or psychiatric disorders, nevertheless other systemic complications as hypertension and chronic kidney disease were seen in 10 patients.

All patient – but one - had high levels of delta-aminolevulinic acid and porphobilinogen measured in 24 hours urine collection. 10 out of 20 female patients were treated with induced menopause lasting 1-2 years,. and 4/27 received the treatment of hematin. All patients had ate least one acute attack in the three months.

The median frequency of acute attacks in the last year was 3 times (0–12 times), and the duration of every attack was 8 days (4–20 days). Analgesic dependency to opioid was a problem in 12 patients. Heme therapy was initiated in all patients with remission of the symptoms in most of the patients for more than 6 months in its first use; recurrent attacks followed by repeated heme injections seemed to alleviate symptoms for a shorter period of time.

Orthotopic liver transplant was performed in three patients with recurrent attacks (one of the patients passed away one month after liver transplant due to fulminant heart attack , apparently not related to porphyria).

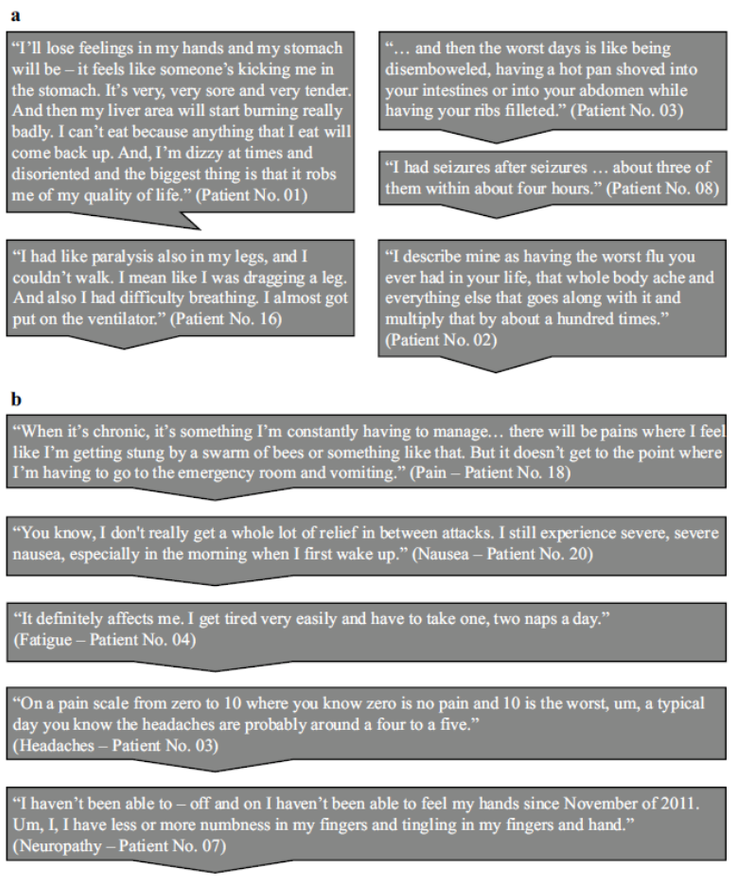

Figure 2 Patients' descriptions of their: a porphyria attacks and b chronic symptoms (extracted from *The Patient - Patient-Centered Outcomes Research (2018) 11:527–537*)

CONCLUSIONS

Our cohort of patients showed frequent recurrent attacks of acute porphyria (>3 per year) requiring in most of them intravenous heme therapy. Although for patients with recurrent attacks prophylactic heme infusions may be benefic in remitting the symptoms, a subset of patients showed less response to this therapy overtime.

Not only facing a debilitating disease state, patients with recurrent attacks can bring a significant burden on health care systems. Acute porphyria patients who suffer from recurrent attacks also report a low quality of life (QoL) and a negative impact on several aspects of everyday life, such as unemployment, personal relationships and long-term disability.

REFERENCES

Scan QR Code and access the references.