Clinical and genetic study of leukodystrophies in Tunisian cohort

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INTRODUCTION

- Leukodystrophies are hereditary disorders affecting central nervous system white matter (WM) with or without damages in peripheral nervous system (1,2)
- Brain **Magnetic resonance imaging** is the major tool to detect WM abnormalities (2)
- Clinical and radiological correlation can help to provide an accurate diagnosis (2)
- Confirmation of diagnosis is based on **molecular study** (1,2)
- In Tunisia, **rare studies** had focused on this subject and clinical and **genetic spectrum of LD remain not defined**

OBJECTIVES

- To determine the clinical and mutational spectrum of Tunisian patients with LD without apparent biochemical markers
- To implement a targeted diagnostic strategy for the most frequent forms

MATERIALS AND METHODS

- Descriptive, longitudinal and prospective study over 5 years (2014-2019) which included all the patients followed for "leukodystrophy"" defined as bilateral, symetrical and confluent involvement of the WM
- We expertized the patient files with a clinical and radiological correlation and we carried out molecular investigations by targeted sequencing of genes either by the classic Sanger technique or by new-generation sequencing techniques

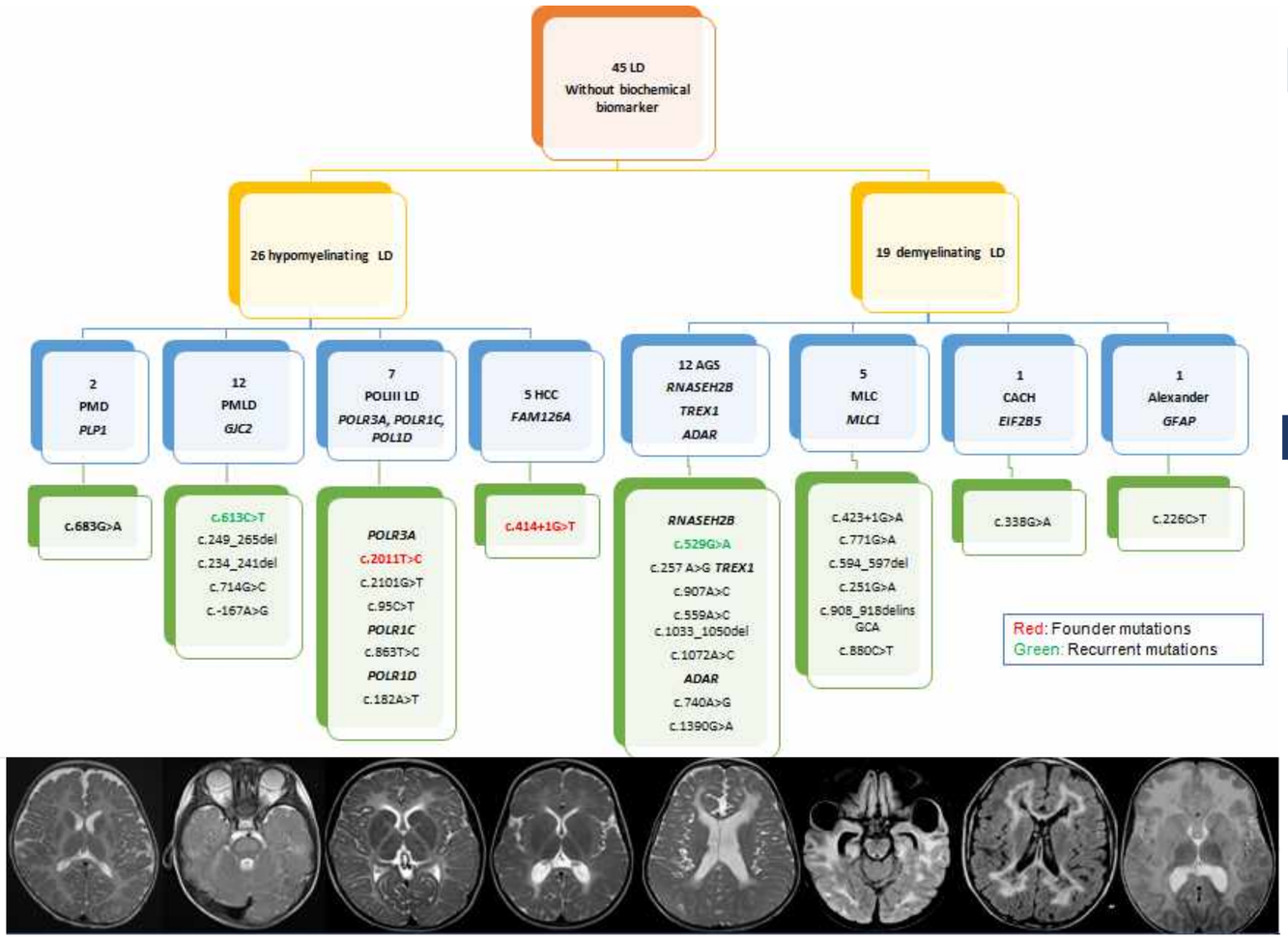

Figure 1: Forms of LD and different mutations identified in our patients

RESULTS

- **45 Tunisian patients** belonging to 39 families with LD without biochemical marker were included
- 26 hypomyelinating LD vs 19 demyelinating LD
- 8 forms of LD (figure 1)
- 27 different mutations (Figure 1)
  - 10 novel mutations
  - 2 founder mutations
  - 2 recurrent mutations

DISCUSSION AND CONCLUSIONS

- Our study contributed to a better knowledge of leukodystrophies in Tunisia and focused on the strong clinical, genetic and mutational heterogeneity of these conditions
- In our study, we identified a novel form of hypomyelinating leukodystrophy by impairing biogenesis of RNA polymerase III related to a homozygous mutation of the *POLR1D* gene described only with Treacher Collins syndrome (3)
- Identification of novel, recurrent, and founder variants is crucial for targeted research, patient's care and genetic counselling

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