Genetic counseling of the idiopatic pulmonary fibrosis in the University Hospital of Liège

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Introduction

Since October 2020, Idiopatic Pulmonary Fibrosis (IPF) patients have been referred by their pulmonologist to genetic consultation when certain criteria were met in their history such as a young age at diagnosis (<60 years old), family history of IPF or personal history suggestive of telomeropathy. Telomeres length was first evaluated by flow fish: patients presenting short telemores underwent a telomeropathies gene panel[1] while patients presenting normal lengths were tested by the IPF gene panel[2]. The aim of this study is to characterize IPF patients seen in genetics consultations and to evaluate our testing strategy.

Methods

We performed a retrospective observational study of the patients from the University Hospital of Liège who had come to a "IPF genetic consultation" between October 2020 and December 2023. We made a descriptive statistical analysis of demographic and clinical characteristics including : reason for referral, age at diagnosis, gender, signs of telomeropathy, family history, as well as the prescribed complementary tests.

Results

We have seen 42 patients : 28 males and 14 females. 33 patients were symptomatic, with a mean age at diagnosis of 63 years (± 8years), 8 patients were IPF first-degree relatives and 1 case was an incidental finding.

Nine patients had clinical signs of telomeropathy : 8 developed early-onset canities, 4 had a personal history of cancer and 3 had signs of myelodysplasia. Five patients had family history of IPF and 10 had family history of cancer.

All 42 patients underwent telomere length testing : 10 patients presented short telomeres and 4 received a result in the grey zone. These 14 patients benefited from the telomeropathies gene panel, carried out at UCL, for which 4 patients received a positive result (Table 1). This panel includes the following genes: *ACD, CECR1, CTC1, DKC1, DNAJC21, ERCC6L2, GAR1, GATA2, MPL, NAF1, NHP2, NOP10, PARN, PGM3, POT1, RMRP, RTEL1, SAMD9, SAMD9L, SRP72, STN1, TERC, TERF2IP, TERT, THPO, TINAG, TINF2, TPP1, USB1, WRAP53, ZCCHC8.* The mutations identified in our four patients are shown in the table below (Table 2).

A further 14 patients benefited from the IPF gene panel, carried out at KUL. It includes the following genes : *ABCA3, ACD, CSF2RA, CSF2RB, DKC1, GATA2, GBA1, HPS1, HPS4, NHP2, NKX2-1, PARN, RTEL1, SFTPA1, SFTPA2, SFTPC, SLC34A2, SMPD1, TERC, TERT, TINF2 + MUC5B.* All these analyses have come back negative for the moment (some tests are still ongoing).

Table 1 : Genetic analysis results

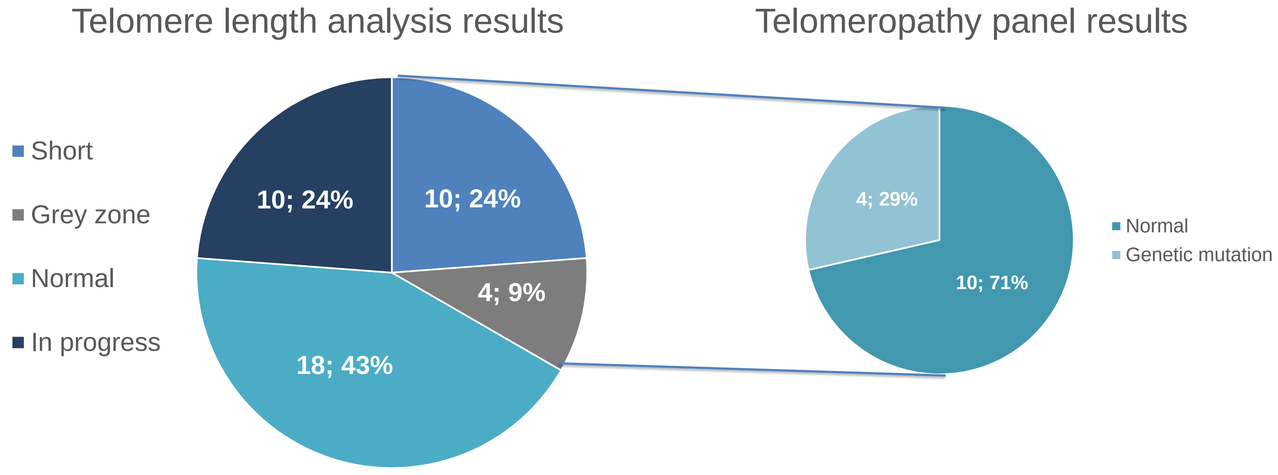

Table 2 : Identified mutations

Gene	Mutation found
PARN	c.157_158del
WRAP53	c.1035C>G
TERT	c.2225G>A
RTEL1	c.2992C>T

Conclusion

We identified an established genetic explanation for 10% of the evaluated patients (4 out of 42). In six additional patients a short telomeres length was detected with no telomerase related genes mutation. Genetic counseling of these partially unsolved cases remains challenging.

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