CO-02

BRUGADA SYNDROME: A 9 YEAR RETROSPECTIVE ANALYSIS

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Brugada syndrome (BrS) is a common familiar arrhythmia syndrome with an estimated prevalence of 1-5 per 10 000 persons. It is characterized by a right ventricular conduction delay, dynamic or persistent ST-segment elevations in the precordial leads V1–3, and an elevated risk of syncope and sudden cardiac death in young adults without structural heart disease.

BrS is an important differential diagnosis for syncope and sudden cardiac death in young adults without structural heart disease.

It is a genetic disease with an autosomal dominant pattern of inheritance and incomplete penetrance. To date, changes in at least 16 genes have been linked with BrS. The Na+ channel gene *SCN5A* mutations are the most frequent, present in 20% to 30% of patients. The other associated genes represent rare sporadic patients or individual BrS families.

We present a nine year retrospective review (between the years 2006 and 2015) of BrS patients from our Medical Genetic Unit, at a tertiary hospital. The study included 41 families, a total of 63 patients, 41 males (65%). Twenty-two out of forty-one families have a clinical diagnose without molecular confirmation (54%) and four families (a total of 15 patients) had molecular confirmation (9,8%), all in *SCN5A* gene. Eight patients were observed due to BrS family history and seven patients following diagnostic suspicion.

Confronting our results with the literature, our molecular confirmation rate is below the expected. We would like to discuss what could justify this findings and what could be done in order to improve the outcome.

CO-03

FABRY DISEASE IN PORTUGAL – INSIGHTS FROM THE MALE PATIENTS

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Introduction: Fabry disease (FD, MIM #301500) is a rare X-linked metabolic disorder with progressive multisystemic clinical course, caused by partial or complete deficiency of α-galactosidase A (α-Gal A), a lysosomal enzyme encoded by *GLA* gene mapped at Xq22.1. The enzymatic defect leads to progressive lysosomal accumulation of the glycolipid globotriaosylceramide in most organs. Clinically, Fabry patients may be divided into two groups: classic and atypical, depending on the age, symptoms and organs involved at diagnosis. The diagnosis in males is based on a deficient α-Gal A enzymatic activity in plasma, leucocytes or dried blood spot, and/or identification of a pathogenic mutation. Reports tend to establish a correlation between the severity of the disease and the degree of α-Gal A deficiency. This work aims to characterize Portuguese FD male patients according to clinical, geographical, biochemical and genetic profile.

Methods: As national reference centre, our laboratory tests most Portuguese FD patients. We performed a retrospective analysis concerning the laboratory determinations, age at diagnosis, district of origin and the main clinical manifestation (according to medical speciality that requested the study).

Results/Discussion: Our cohort includes 80 male patients belonging to 50 different families, being Braga the district with a higher frequency.

Our results revealed a mean age of index cases at diagnosis of 46 years-old, the sixth decade of life the most representative age interval and p.F113L the most prevalent mutation. These facts seem to be correlated, as this mutation is associated with FD late-onset cardiac variant and most patients were studied upon Cardiology request. According to some authors, patients carrying p.F113L mutation are expected to have a high residual enzyme activity; nevertheless our results evidence a severe enzyme deficit (7.3% of the minimum of the control range).

Hereto, we describe three novel genetic variants – c.386T>G (p.L129R), c.607G>T (p.E203*), c.683A>G (p.N228S), besides other puzzling cases.

Conclusion: Due to the prevalence of p.F113L mutation in this FD patients cohort, the authors observed a bias, namely in the age of diagnosis and the clinical variant, when compared with other reports. Furthermore, this study provides an extremely useful tool to establish orientations for an earlier diagnosis, more efficient treatment management and appropriate genetic counselling of patients and their families.