Mitochondrial mutation in adult patient with Hypertrophic Cardiomyopathy and renal failure

C. Mazzaccara[1], G. Frisso[1], G. Limongelli[2], R. Calabrò[2], F. Salvatore[3]

[1]CEINGE-Biotecnologie Avanzate s.c.ar.l, Napoli, Italy e Dipartimento di Medicina Molecolare e Biotecnologie Mediche, Università di Napoli Federico II, Napoli, Italy; [2]Cardiologia SUN, Ospedale Monaldi, Azienda dei Colli, Seconda Università di Napoli, Napoli, Italy;
[3]CEINGE-Biotecnologie Avanzate s.c.ar.l, Napoli, Italy e IRCCS-Fondazione SDN, Napoli, Italy.

Background: Mitochondrial diseases (MDs) (1:5000-10000) represents a wide group of human disorders associated with mitochondrial DNA (mtDNA) variations causing defect of oxidative phosphorylation system, whereas nuclear genome mutations are somewhat rare. The extremely heterogeneous clinical phenotype, extending from oligosymptomatic condition to complex syndromes involving neurological, ophtalmological, gastroenterological and endocrine features, depends to the involved tissue well as to the specific mtDNA mutations and their heteroplasmic level. Diabetes and deafness are common features of mitochondrial diseases, while renal alterations are rarely reported, especially in adults, probably because of lack of association to mitochondrial conventional phenotypes.
Case Presentation: We investigated a 62 years old male affected by hypertrophic cardiomyopathy (HCM) and renal failure that caused already a bilateral transplantation. Pathological anamnesis revealed also diabetes, deafness and Crohn disease. Family history of cardiomyopathy showed a strong mitochondrial involvement. The proband's mother, three brothers (one of which died of renal failure at 26 years), the sister and her child were affected.
Materials and Methods: Genomic DNA from peripheral blood and buccal cells was extracted with the Kit-Nucleon-BACC2 (Illustra DNA-Extraction Kit-BACC2-GE Healthcare, UK) and the whole mitochondrial genome was amplified by two pair of primers designed in our laboratory to generate two overlapping fragments. The PCR products were then sequenced and compared to mitochondrial reference sequence (rCRS NC_012920).
Results and Discussion: In both biological samples the mtDNA analysis showed the heteroplasmic A3243G mutation in the $tRNA^{Leu\ (UUR)}$, frequently associated with MDs.
A cardiological involvement leading to hypertrophic remodelling, caused to mitochondria intermyofibrillar proliferation, occurs up to 40% of patients with mtDNA disease. Molecular backgrounds of mitochondrial cardiomyopathy of adult age are still quite poorly known and the A3243G mutation in $tRNA^{Leu(UUR)}$ of mtDNA has been reported in 40-60% of patients with HCM.
The interesting finding presented here support the knowledge that mitochondrial gene altertation represents a possible etiology in cardiological patients with unexplained renal failure. This is particularly true, as in this case, when other associated symtoms linked with dysfunctional oxidative phosphorylation are present.
The case presented in this report further suggests that a differential diagnosis in presence of HCM should be solved by a multidisciplinary approach together with mutation analysis of mitochondrial DNA.

Keywords: Hypertrophic Cardiomyopathy, Mitochondrial Diseases, Renal failure

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