INCIDENTAL FABRY'S DISEASE DIAGNOSIS IN NEPHROLOGY UNIT

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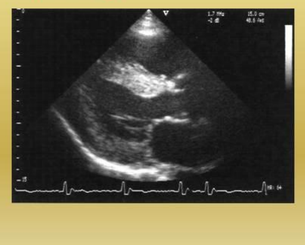
On behalf of Cardionephrology Study Group of Italian Society of Nephrology



Background - 1

Fabry's disease (FD) is a devastating progressive inborn error of metabolism with lysosomal glycosphingolipid deposition in variety of cell types, capillary endothelial cells, renal, cardiac and nerve cells.

Basic effect is absent or deficient activity of lysosomal exoglycohydrolase agalactosidase A.

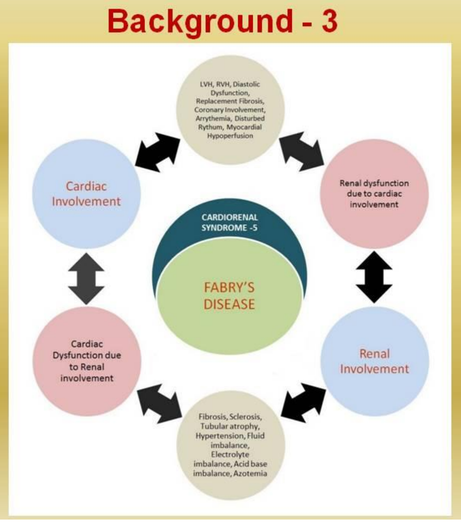
Renal involvement consists of, proteinuria, isosthenuria, altered tubular function, presenting in second or third decade leading to azotemia and end stage renal disease in third to fifth decade mainly due to irreversible changes to glomerular, tubular and vascular structures, especially highlighted by podocytes foot process effacement.

Cardiac involvement consists of left ventricular hypertrophy, right ventricular hypertrophy, arrhythmias (sinus node and conduction system impairment), diastolic dysfunction, myocardial ischemia, infarction, transmural replacement fibrosis, congestive heart failure, and cardiac death

Background - 2

Organ System		Sign/Symptom
Nervous System		Acroparesthesias, Nerve Defness Heat Intolerance, Hearing Loss, Tinnitus
Gastrointestinal		Nausea, Vomiting, Diarrhoea, Post-prandial bloating /pain, Early satiety, Difficult weight gain
Skin		Angiokeratomas, Hypohidrosis
Eyes		Corneal and lenticular opacities, vasculopathy (retina, conjunctiva)
Kidneys		Microalbuminuria, Proteinuria, Impaired concentration ability, hyperfiltration, ↑ uGb3 excr.
Heart		Impaired Heart Rate variability, Arrythmias, Short P-R interval, Mild Valvular Insufficiency

Background - 3



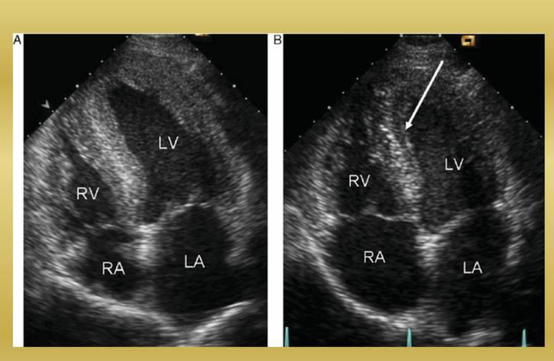
Patients and Methods

- ✓ 85 patients (45 males and 40 females) have been enrolled with a mean age of 45 ± 3 years, followed by single nephrology department outpatient unit.
- ✓ All patients underwent trans – thoracic echocardiography and those with stable cardiomiopathy were excluded (n= 35)
- ✓ All remaining patients with left ventricular hypertrophy and without diagnosed cardiopathy were asked to undergo screening test for Fabry's disease

Results

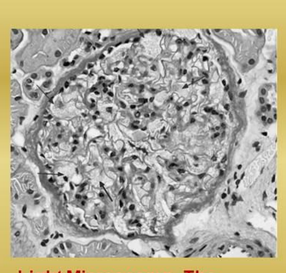
- ✓ Among remaining 50 patients (20 males and 30 females), 30 of them showed an unespected hypertrophic cardiopathy.
- ✓ All 30 patients underwent further investigations: proteinuria (n= 30) and anamnestic cerebrovascular disease (n=2) were also found.
- ✓ After screening test, four patients were accountable for Fabry's disease; genetic assay (GLA gene mutation) confirmed preliminary results

Fig. 1 – Left ventricular hypertrophy



LVH in Fabry's Disease: arrow indicates typical binary appearance

Fig. 2 – Urinary findings



Light Microscopy: The glomerular podocytes are swollen and finely vacuolated (arrows) in a patient with Fabry nephropathy disease (PASx40)

Electron microscopy. Lamellated lipid inclusions (zebra bodies) in a podocyte cytoplasma (UrPb X 40.000.)

Conclusions

- ✓ Fabry's disease diagnosis is often underated and actual incidence is unknown at present time.
- ✓ Correct evaluation of instrumental and serological tests is crucial: combined evidence of proteinuria and hypertrophic cardiomiopathy can allow to perform a Fabry's disease diagnosis
- ✓ Nephrologists who perform echocardiography could be helpful in discriminating left ventricular hypertrophy in patients with cardiomyopathy and/or chronic kidney disease by those in which echocardiographic features cannot be explained.

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