Continuing Education

MODULE 17: *Cardiology*

PART 3

Anderson-Fabry disease in young people

by Helen O'Donnell

ANDERSON-FABRY disease (more commonly known as Fabry disease) is a rare X-linked recessive metabolic disease that can affect a lot of systems within the body. It is estimated to affect one in 40,000 males.[1,2] It was discovered in the 19th century by a German physician called Johann Fabry and an English physician called William Anderson. It is an inherited lysosomal storage disorder.

As this is a metabolic disorder, it can affect almost every cell in the body causing multiple systems to be affected. It is caused by a defect on the gene that codes for the production of the enzyme α galactosidase A. This results in the inability to break down glycosphingolipid-globotriaosylceramide (GL-3) which is a normal product of metabolism.[3] This then accumulates in the endothelial and visceral tissues affecting the major organs such as the kidneys, the heart and the brain.

As Fabry disease is X-linked the condition is typically inherited through the mother. An affected mother will have a 50% chance of passing on the defective gene to both males and females. If she passes on the gene to her son they will be affected and if she passes the gene on to her daughter they will be carriers. However female carriers can also present with many clinical manifestations of Fabry disease. Males that are affected cannot pass this condition onto their sons, but every daughter they have will be a gene carrier *(see Figure 1)*.

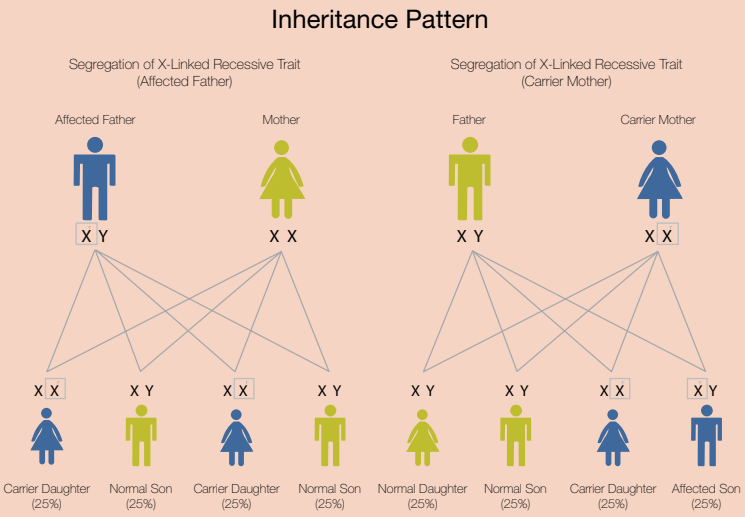
Clinical presentation

The clinical diagnosis of Fabry disease can be a difficult one to make as the presentation and progression of the condition varies. Symptoms can appear in childhood and include: pain, fatigue, intolerance to heat and cold, recurrent fever, mild proteinurea and many more. Shelly et al[4] state that many of these symptoms can go unnoticed at first. These symptoms can be broken down into the different systems that are affected.

- *Pain:* Pain is one of the early symptoms. Typically Fabry pain is present in the hands and feet and radiating inwards which can last from minutes to weeks[3]

Figure 1

Inheritance pattern for Fabry disease



- *Angiokeratoma:* These are cutaneous lesions, reddish in colour, non-blanching and are mostly present in the groin, buttocks, umbilicus and the upper thighs ('bathing- trunk' distribution). These may also be present with other lysosomal storage disorders[3]
- *Ocular findings:* Asymptomatic corneal opacities are common with Fabry's[3]
- *Renal:* Patients may develop proteinurea in late adolescence which progressively worsens[3]
- *Cerebrovascular:* Ischaemic stroke is quite common in Fabry disease.[1] Rolfs et al state that Fabry disease can account for around 1-2% of young stroke patients[7]
- *Cardiac:* Cardiac involvement varies. If it is present its severity will worsen with age. This includes left ventricular hypertrophy (LVH), ischaemic heart disease (IHD), conduction abnormalities, myocardial infarction (MI), arrhythmias and mitral valve insufficiency.[3] It accounts for around 3% of unexplained LVH in middle aged men.[9] Up to 2% of patients diagnosed with hypertrophic cardiomyopathy have been found to have Fabry disease as the underlying cause.
- *Gastrointestinal:* These symptoms include diarrhoea, pain, bloating, weight loss and nausea.

Fabry disease leads to multi-organ dysfunction and premature mortality, therefore early recognition and treatment is essential.

Diagnosis

Family history is essential in making a diagnosis. Early strokes, renal and cardiac disease, with a pattern of males being almost exclusively being affected, could indicate a possibility of Fabry disease.[3] Diagnosis is based on clinical features, family history and α galactosidase A enzyme levels via a blood spot test which is

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Symptoms of Fabry disease

Early features	Late features
Pain	Renal failure
GI symptoms	Cardiac complications
Cold/ heat intolerance	Stroke
	Death

preformed in Manchester. Fabry disease is still under-diagnosed with the average delay from onset of symptoms to diagnosis is more than a decade.[8]

Treatment

The therapy involves replacing the enzyme responsible for Fabry disease and it is given as an intravenous infusion. There are two enzyme replacement therapies that are currently used in Ireland.

One of the enzymes used is agalsidase beta (Fabrazyme). This replaces the missing enzyme leading to the clearance of GL-3. It is given as a dose of 1mg/kg every two weeks.[1] It has been shown to reduce the risk of cardiac, renal and cardiovascular events by 61%.[9] The cost of this enzyme replacement is over €4,000 per 35mg vial.

The other therapy is called agalsidase alfa (Replagal) and it is given as a 40-minute infusion. This can be done in the home with specialist nurses employed to give the medication and reduce hospital visits. Weidemann et al state that enzyme replacement therapy can reduce LVH and improve regional myocardial functioning.[5]

Nursing care

The nursing care of a patient with Fabry disease needs a holistic approach as this is an inherited condition and may have many psychosocial aspects. Many Fabry patients can show signs of depression, reduced quality of life and feelings of alienation.[6] A specialist genetic counsellor may be required to assist in the development of a family pedigree to help identify other affected family members.

Anderson-Fabry disease is a rare and under diagnosed condition and a delay of diagnosis from the beginning of symptoms can take more than a decade.[8] Patients who present with unexplained pain, unexplained LVH or early stroke and a suggestive family history of Fabry disease should be assessed by a specialist for the possibility of Fabry disease.

Helen O'Donnell is a CNMII in the Cardiac Risk for Younger Persons (CTYP) Centre in Tallaght Hospital

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