Muscular Dystrophy New Zealand

Tarui Disease

Tarui disease (also known as phosphofructokinase deficiency, or glycogen storage disease type VII) was first described in 1965 by the Japanese physician Seiichiro Tarui and his co-workers. It is caused by deficient activity of the enzyme phosphofructokinase (muscle PFK or PFKM) in muscle tissue. Lack of this enzyme means that a complex sugar called glycogen is unable to be broken down. The excess glycogen in the muscle cells causes damage. It is very rare with approximately 100 cases being reported worldwide affecting both males and females. Individuals with Tarui disease experience symptoms such as pain and muscle weakness, and sometimes muscle cramps or spasms, during intense physical activity (exercise intolerance).They may also experience mild jaundice caused by accelerated disintegration of red blood cells. Muscle fatigue usually resolves quickly with rest, but after strenuous activities symptoms may linger for days. The disease can cause muscle pain, cramping and lower back pain, but the severity of symptoms in the muscles varies widely among individuals with the disease.

Varieties and Features of Tarui Disease?

There are four different forms of Tarui disease, which are classed by their signs and symptoms and age of presentation.

1.The classical form is the most common and usually appears in childhood. It is characterized by muscle pain and cramps, often after the person has done some moderate exercise. Strenuous exercise can lead to nausea and vomiting. During exercise, muscle tissue can be abnormally broken down, releasing a protein called myoglobin. This protein is processed by the kidneys and released in the urine (myoglobinuria). If untreated, myoglobinuria can damage the kidneys and lead to kidney failure. Some people with the classical form of Tarui disease develop high levels of a waste product called uric acid in the blood (hyperuricemia) because the damaged kidneys are unable to remove uric acid effectively. Affected individuals may also have elevated levels of a molecule called bilirubin in the blood that can cause yellowing of the skin and whites of the eyes (jaundice). Individuals with classical Tarui disease often have elevated levels of an enzyme called creatine kinase in their blood. This finding is a common indicator of muscle disease.

2.The severe infantile form affects babies who present with low muscle tone (floppiness), the condition leads to muscle weakness that gets progressively worse. Affected children have a weakened and enlarged heart (cardiomyopathy) and difficulty breathing normally. This type of Tarui disease is very serious and individuals usually do not survive past their first year of life, often as a result of infection or breathing problems.

3.The late-onset form typically presents in individuals in their 40s or 50s usually with only the muscle weakness, although some individuals have difficulty with sustained exercise that they noticed starting in childhood. The weakness generally affects the muscles closest to the center of the body (proximal muscles).

4.The hemolytic form is characterized by hemolytic anemia, this is when red blood cells are broken down (undergo hemolysis) prematurely, causing a shortage of red blood cells (anemia). People with the hemolytic form of Tarui disease do not experience any signs or symptoms of muscle pain or weakness related to the disorder. This form is very rare.

Symptoms of Tarui Disease

The symptoms are due to the muscles not having enough energy to function normally. This means the cell has to find other sources of energy and results in muscle cell damage and degeneration. The condition causes pain, cramping, weakness and muscle stiffness in activities involving exertion, such as walking, running, carrying or lifting. In some individuals muscle activity, demanding energy, leads to the breakdown of muscle protein. There may also be an increased production of uric acid, which is the cause of painful inflammation of the joints (gout).

When muscle cells are damaged, myoglobin (a substance which gives muscles their red colour) leaks from muscle cells into the blood plasma. When the blood plasma is filtered through the kidneys the urine becomes red coloured (myoglobinuria). Myoglobinuria is a serious complication requiring acute hospital care, as very high concentrations of myoglobin in blood plasma causes in kidney damage. Some myoglobinuria patients develop acute renal failure requiring dialysis.

An increased rate in the breakdown of red blood cells (haemolysis) can lead to varying degrees of jaundice (icterus). In most cases the condition manifests as a yellow discolouration of the whites of the eyes. Also increased calcium ion content in the red blood cells sometimes ‘upsets’ the cell membranes, which in turn may trigger

the coagulation process resulting in the development of blood clots and cardiovascular complications.

Genetics

Mutations in the PFKM gene cause Tarui disease. The gene codes for a protein which forms one part (the PFKM subunit) of an enzyme called phosphofructokinase. PFKM gene mutations result in the production of PFKM subunits that have little or no function.

The phosphofructokinase enzyme is made up of four parts (made from 3 subunits) which combine in different ways to make 3 different types of functioning enzyme for the muscle, liver, and platelets. In normal muscles used for movement (skeletal muscles) the enzyme is made completely of PFKM subunits, this means that the mutated subunit cannot make a functioning enzyme and the muscle cells cannot break down glycogen into glucose. As a result, partially broken down glycogen then builds up in muscle cells. Muscles that do not have access to glycogen as an energy source become weakened and cramped following moderate strain, such as exercise, and in some cases, begin to break down.

However, in red blood cells there is a mixture of enzyme types which means that there is only a partial absence of the enzyme in these cells, approximately 50 per cent. Glycogen is also found and broken down in the liver but the PFKM subunit is not a subunit of liver phosphofructokinase which is why the liver is not affected by Tarui disease.
Swedish researchers have identified an association between PFKM deficiency and increased leakage of calcium ions into red blood cells. The abnormally high concentration of calcium ions reduces the elasticity of the red blood cell membranes, which is probably the direct cause of the accelerated disintegration of red blood cells (haemolysis) and jaundice in patients with Tarui disease.

Inheritance

This condition is inherited in an autosomal recessive pattern. We all have two copies of each chromosome except for the sex chromosomes. In recessive conditions both copies of the gene must be defective for the disease to develop fully. In this situation each parent is a carrier of one defective gene. And in each pregnancy they have a 25% chance of have a child affected with the condition.

Genetic counseling is available to families who have had a diagnosis of Phosphofructokinase deficiency. This service provides information, helps families understand inheritance patterns and what this means in their family, as well as

enabling people to make more informed family-planning decisions. You can access this via your GP, self-refer or an MDA Fieldworker can assist you.

Diagnosis

• An investigation should be carried out to exclude other possible causes of jaundice. The diagnosis is then established by analysing phosphofructokinase enzyme activity in the red blood cells. Usually, the test results show slightly lowered activity.

• Glycogen and the Phosphofructokinase subunit concentrations are measured in a microscopic analysis of biopsied muscle tissue, usually taken from the outer thigh.

• DNA-based diagnostics can be used to identify the PFKM mutation is some circumstance.

Management

There is currently no cure for Tarui disease, but various treatments may alleviate symptoms and complications.

Individuals with Tarui disease should be observant to myoglobulinuria, presenting as a dark discoloration of the urine. Owing to the risk of kidney damage, medical help should be sought immediately if symptoms arise. Dialysis is sometimes needed if toxic waste products have accumulated in blood plasma (uraemia).

Jaundice is generally mild and does not require treatment.

Individuals affected by recurrent blood clotting should undergo a blood coagulation investigation and may require anticoagulant medication.

High uric acid concentrations that may cause gout can be treated with drugs that lower uric acid levels in the blood.

The effectiveness of dietary management remains unclear. It is possible that food with a high fat content, notably fatty fish, has a beneficial effect, as the glycerol (glycerine) in neutral fat can replace glucose as a better source of energy. It may be possible to accustom the skeletal muscle cells to oxidise fatty acids rather than glucose to produce energy.

Muscular Dystrophy New Zealand

Individuals with Tarui disease should avoid intensive muscle activity. It is not recommended to avoid all physical activity to prevent the exercise intolerance symptoms as physical inactivity has many negative consequences for physical and mental health. Individual advice and help with designing a suitable exercise programme can be provided by a physiotherapist. People with this condition can usually carry out household work and jobs not requiring strenuous muscle effort, although all activities must be adapted to the limitations imposed by reduced muscle functionality. It is recommended that an occupational therapist be consulted to be sure that all appropriate aids are available to assist.

It is important that preschool and school staff are informed about the condition, with suggestions about suitable physical activities. These should be adapted to suit the individual needs of the child.

Most people with the disease live normal lives as long as they avoid intensive muscle activity, and the need for treatment is highly individual. It is important to avoid occupations requiring a great deal of physical exertion.

Support

The MDA Fieldworkers are available for support. They have in-depth knowledge of a range of neuromuscular conditions, and will have a better understanding of your needs and challenges. Have a chat over the phone or they can come to you for a kanohi ki te kanohi/face-to-face visit. They may have some real practical suggestions that have worked for others to offer as well. This service is offered free of charge to MDA members and is funded through donations and grants. Contact your local MDA Branch to be put in contact with your fieldworker.

The MDA Support Network allows people with similar circumstances or challenges to come together to share their experiences and provide each other with emotional and moral support in addition to practical advice and information. By bringing together people with common experiences, support networks can provide an invaluable addition to medical care. The MDA of New Zealand Support Network currently has over 700 members throughout New Zealand who want to be in touch with others livings with neuromuscular conditions. Please see the MDA website www.mda.org.nz for contact details and more information that you might find relevant for you and your whanau..

Muscular Dystrophy New Zealand

Sourced from
http://ghr.nlm.nih.gov/condition/glycogen-storage-disease-type-vii
http://www.socialstyrelsen.se/rarediseases/taruidisease
https://rarediseases.org/rare-diseases/glycogen-storage-disease-type-vii/
http://www.livestrong.com/article/415921-what-happens-when-your-body-runs-out-of-glycogen-during-a-longworkout/
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=371