Abstract

My report will have to discuss a type of neurological disease adrenoleukodystrophy refers to several different inherited condition that affect the nervous system and adrenal gland.The three major categories of ALD are childhood cerebral ALD ,adrenomyelopathy and Addison's disease.The gene that causes ALD was identified in 1993.According to the oncofertility consortium ALD occurs in about 1 in 20,000 to 50,000 people and mainly affects men.Women with the gene tend to be asymptomatic or mildly symptomatic ,meaning there are no symptoms or very few symptoms.The symptoms,treatmeants,and prognosis of ALD very depending on wich type is present.ALD is not curable,but doctors can sometimes sow its progression.

Introduction

Adrenoleukodystrophy;is an X-Linked metabolic disorder characterized by the breakdowen or loss of the myelin sheath surrounding nerve cells in the brain and progressive dysfunction of the adrenal gland .Adrenaleukodystrophy is one of a group of genetic disorders called the leukodystrophies that cause damage to the myelin sheath of the nerve fibres in the brain.The myelin sheath is a fatty covering which acts as an electrical insulator(5).Without that sheath the neurons cannot conduct action potentials-in other words they stop telling the muscles of ther elements of the central nervous system what to do.This sequence of events appears to be related to an abnormal accumulation of saturated very long-chain fatty acids(VLCFA)in the serum and tissues of the central nervous system,which sets off an abnormal immune respose that leads to demylination it is unclear exactly how this chain of events works,but scientists do know that it has its roots in genetics.(6)

Discussion

Main type of ALD

1-Childhood cerebral;This is the most common form of adrenolukodystrophy.It is usually found in males.This type of ALD starts in childhood,most often between the ages of 3 and 10 years old.It progresses very quickly and causes deterioration in the brain.

The most common symptoms are behavior changes(such as with drawal and aggression),memory problems,and performance at school.

Other signs and symptoms may include;

Hearing or speech problems ,including deafness, seizures, difficulty swallowing, vomiting, walking and coordination problems, tiredness, progressive dementia and skin pigmentation

2-Adrenomyeloneuropathy(AMN)

Most other people with ALD and AMN .This type of ALD presents later in life,usually in the person's 20s or 30s,and mainly affects men.It is less severe than childhood cerebral ALD,progressing more slowly in comparision.It can lead to moderate or severe disability over a number of years.This type of ALD causes damage to the

nerves that communicate between the brain and limbs,so symptoms include stiffness,weakness and paralysis of the lower limb.Patients may also have problems with coordination,balance an speech(sometimes called ataxia)

3- **Addison's disease**

Most people with childhood ALD and AMN have Addison's,which has symptoms including tiredness,musclkness,depression,low appetite and increased thirst.This disorder affects the adrenal gland,which produces hormones to control the levels of sugar,salt and potassium in the body.These essential hormones are called cortisol and aldosterone.People with Addison's disease do not produce enough cortisol and aldosterone because the gland is damaged.This aspect of the condition can be treated with a daily dose of medication to replace the missing hormones.

X-linked adrenolukodstrophy

Causes

X-linked adrenoleukodystrophy (X-ALD) is caused by a variation (mutation) in the *ABCD1* gene. This geneprovides instructions to make a protein called the adrenoleukodystrophy protein (ALDP). ALDP normally moves a type of fat molecule called very long-chain fatty acids (VLCFA) into a special part of the cell to be broken down. When the *ABCD1* gene is changed, there is too little ALDP in the cells or the ALDP that is made does not work normally. This causes VLCFA to build up in the body. High levels of VLCFA are thought to be damaging to the outside of the adrenal glands (adrenal cortex) and the fatty covering (myelin) that surrounds the nerve cells in the brain and spinal cord. Researchers believe the damage caused by VLCFA may involve inflammation, especially in the brain.[1][2]

Inheritance

X-linked adrenoleukodystrophy (X-ALD) is inherited in an X-linked manner.[1] This means that the *ABCD1* gene is located on the X chromosome. The X chromosome is one of the sex chromosomes. Each woman has two X chromosomes, and each man has one X chromosome and one Y chromosome. Because men have only one X chromosome, they only have one copy of the *ABCD1* gene. If this gene has a disease-causing change, they will have X-ALD. Women who have disease-causing changes in one copy of the *ABCD1* gene are known as carriers of the disease. About 80% of carriers do not have signs or symptoms of X-ALD because they have another working copy of *ABCD1*. However, about 20% of female carriers have symptoms that are similar to the adrenomyeloneuropathy (AMN) type of X-ALD.[2]If a male is diagnosed with X-ALD, it is likely that his mother is a carrier of the disease. However, about 5% of cases of X-ALD are caused by a new genetic change (de novo) in the individual. In these situations, the mother is not a carrier of the

disease, and other family members are not at risk to have children with X-ALD. Therefore, when a male is diagnosed with X-ALD, it is important to determine if his mother is a carrier by testing her VLCFA levels or by genetic testing.[2] If a woman is found to be a carrier of X-ALD, for each of her children there is a 50% chance that he or she will inherit the change in *ABCD1*. This means that for each son, there is a 50% chance that he will be affected with X-ALD. For each daughter, there is a 50% chance that she will be a carrier of the disease like her mother.X-ALD shows a characteristic known as variable expressivity. This means that the exact symptoms of each person with X-ALD can differ, even within the same family. For example, some boys may have the childhood cerebral form of X-ALD, while other members of the same family may have the adrenal insufficiency-only type.[2]It is not known what causes variable expressivity of the disease to occur. The symptoms cannot be predicted by levels of VLCFA or by looking at the exact genetic change (mutation) in each individual.[2]

studies

1- A study of children attending the Metabolic Unit at El-Khadra Teaching Hospital (MUKH) in Tripoli, took place between 1st January 2001 and 31st December 2012. Over the 12-year study period of which 107 patients were diagnosed with 46 different types of Inborn errors of metabolism (IEM) diseases. The total number of live births at El-Khadra Hospital was 55,422. Consanguinity rate was 86.9% among parents of affected children. Thirty-three patients died. Twelve families had two affected children. Family history of previously affected children was noted in 63.5% of cases. Family history of infantile death with similar illnesses was 52.3% (56 families). One effected child reached adulthood at the end of the study period. The sex distribution was 58 males and 49 females The most frequent disorders were amino acid (25%), carbohydrate (14.9%), lysosomal storage disease (14%), organic acids and energy defects (9.3% each).

2- Retrospective study evaluating the data of 10 X-linked adrenoleukodystrophy patients diagnosed at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia.The common presenting symptoms were deterioration in school performance, vision and hearing, behavioral changes, and seizures. Eight patients survived 1-4 years and one patient 12 years after the initial presentation, while one patient expired. Six patients had the childhood form, 3 had the adolescent form and one had the adrenomyeloneuropathy form. Six are in an advanced stage of the disease and 3 have mild to moderate spasticity. All except 2 manifested moderate to severe dementia with variable degrees of visual loss. Decreased hearing and features of adrenal insufficiency were seen in 7 patients. Very long chain fatty acids were significantly increased in seven and mildly elevated in 2 patients.

conclusion

X-linked adrenoleukodystrophy (X-ALD) is a genetic disease that affects the nervous system and the adrenal glands (small glands located on top of each kidney). People with this disease often have progressive loss of the fatty covering (myelin) that surrounds the nerves in the brain and spinal cord. They may also have a shortage of certain hormones that is caused by damage to the outer layer of the adrenal glands (adrenal cortex). X-ALD is caused by a variation (mutation) in the *ABCD1* gene and it is inherited in an X-linked. manner. Diagnosis of the disease is based on testing the levels of a molecule called very long-chain fatty acids

(VLCFA).The diagnosis can be confirmed with genetic testing. There is still no cure for X-ALD, but taking special oils such as Lorenzo's oil can lower the blood levels of VLCFA. Bone marrow transplantation may be an option for boys who have evidence of brain involvement on MRI.

References

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