Information sheet on Activated PI3K delta syndrome (APDS)

What is APDS?

Activated PI3K delta syndrome (APDS) is a rare primary immunodeficiency. About 30–40 people in the UK are known to be affected by the condition. First discovered in 2013, APDS is an inherited disorder that affects both males and females. People with APDS are more prone to viral and bacterial infections because of problems with their immunity.

What causes APDS?

APDS is caused by changes in the PIK3CD (APDS1) or PIK3R1 (APDS2) gene that control the production of phosphoinositide 3-kinase delta (PI3K delta). This protein is important for the certain white blood cells (B-cells and T-cells) to function.

What are the signs and symptoms of APDS?

People with APDS may present in childhood or later in life with severe, persistent, or recurrent bacterial and viral infections (usually in the lungs, nose or ears), with a persistent phlegmy cough. They can also have problems with glandular fever, cold sore and chickenpox viruses.

Patients might have signs of autoimmunity and excessive inflammation, leading to anaemia, easy bruising, inflammatory bowel disease, or kidney inflammation. They may also suffer from swollen glands and often an enlarged spleen and liver. Although often benign, APDS is also be associated with lymphoma.

How is APDS diagnosed?

The diagnosis of APDS is based on the signs or symptoms that an individual has, laboratory tests and genetic testing. As it is a rare condition, diagnosis might be delayed. The key to accurate diagnosis is the genetic tests.

How is APDS treated?

The treatment(s) depends on the individual's symptoms and is tailored to each person's health needs. If you have APDS, your specialist health team will discuss with you the treatment options that may be beneficial to you.

Infections can be managed with antibiotics. Some patients are given regular (prophylactic) antibiotics to try and prevent recurrent infections. Other supportive treatments include breathing exercises and chest physiotherapy.

For people with low immunoglobulin (antibody) levels, immunoglobulin replacement therapy may be recommended. The aim of immunoglobulin replacement therapy is to prevent infections and offer protection from possible further infections that can result in damage to organs, such as the lungs.

Drugs, such as steroids and other immune suppressants or biologics can be used to treat patients with excessive inflammation.

'Targeted therapies' are becoming available (clinical trials ongoing) that specifically target the overactive PI3K delta enzyme. These are known as PI3K delta inhibitors, and they may prove potentially useful in the treatment of conditions linked with the excessive production of white blood cells (lymphoproliferation).

Bone marrow transplantation (BMT) is a potential cure for APDS. If HSCT is offered, then the risks will be discussed fully with the patient by the specialist transplant team.

Patients' health will be monitored regularly.

The genetic inheritance of APDS and family planning

APDS can affect both males and females. In most people with APDS, a single copy of the faulty gene is passed on from one parent and a normal copy from the other parent. This is a pattern of inheritance called autosomal dominant inheritance. Sometimes new genetic changes can occur unexpectedly in people with no history of the disorder in their family. If the genetic change occurs at the time of conception (in the egg or sperm), then it is considered 'sporadic' and the disorder could pass to the next generation.

All offspring of an individual affected with APDS have a 50% (1 in 2) chance of inheriting the abnormal gene and being affected by the disorder. The risk is the same for every pregnancy, so family planning is an important consideration and genetic counselling is recommended. All family members of a person with a confirmed diagnosis of APDS should be genetically tested. While family members may not have the same symptoms or any symptoms, they may still carry the genetic condition and pass it onto their biological children.

For more information, please read our leaflet 'Genetic aspects of primary immunodeficiency'.

Reference

Activated PI3 Kinase Delta Syndrome: From Genetics to Therapy - PMC (nih.gov)

Patient stories

Bethany's story

Jamie's story

FAQs

Q. Does having APDS affect body systems other than the immune system?

A. The enzyme PI3K is present in all body tissues. This means that APDS can affect functions outside of the immune system, including the central nervous system causing developmental delay.