Alpha-1 Antitrypsin Deficiency

Alpha-1 antitrypsin deficiency is a disease caused by a reduction of Alpha-1 antitrypsin in the body. Alpha-1 antitrypsin is an enzyme. Alpha-1 antitrypsin deficiency is a common inherited (*genetic)* deficiency in white (*Caucasian*) populations. Both males and females are at risk.

CAUSES

Blood and tissues have an inhibitor (controller) of this enzyme that prevents harmful activity. The most common protease inhibitor in the blood is alpha-1 antitrypsin, and its job is to protect the tissues from protease attack. These proteins play an important role in controlling inflammation, blood clotting and mechanism repair in the body. Most alpha-1 antitrypsin in the body is produced by the liver. The liver and lungs are damaged by a shortage (*deficiency*) of this enzyme.

In the lungs, alpha-1 antitrypsin deficiency produces a chronic progressive lung disease (*emphysema*). The lack of alpha-1 antitrypsin leads to lung damage that gets worse (*progressive*) by protease enzymes, especially when combined with other factors such as smoking. The disease often becomes noticeable between the ages of 30-40 years in smokers, and 10-15 years later in nonsmokers. Over the next 15 -20 years, the lung disease may gradually lead to breathing (*respiratory*) failure and death.

The progress of liver disease is less predictable. Alpha-1 antitrypsin deficiency can produce jaundice and liver problems in babies within days of their birth. Some babies may develop a quickly worsening condition, although symptoms often improve. A few children with alpha-1 antitrypsin deficiency develop significant liver disease before the age of 20. Liver problems due to alpha-1 antitrypsin deficiency may only become known about in adult life. But few people, even those with the severe genetic variant, develop cirrhosis or liver scarring. The progress of liver disease is not predictable.

SYMPTOMS

People with emphysema, especially smokers, complain of shortness of breath and a cough. This shortness of breath first occurs only during activity or exercise, but can lead to difficulty breathing when at rest. This usually occurs over 15-20 years, but can lead to breathing failure and early death.

Alpha-1 antitrypsin deficiency is the most common genetic or inherited cause of liver disease in infants and children. The first signs are often jaundice, pale stools, excessive bleeding, or an enlarged liver - all nonspecific signs of liver disease. This usually begins between 4 days and 6 weeks after birth. A few babies rapidly develop liver failure and cirrhosis. Most infants will improve. Urgent treatment may not be required. In later childhood, patients may develop signs of chronic liver disease and liver failure. The symptoms are:

- Abdominal pain.
- Jaundice.
- Enlargement of the liver or spleen.
- Itching.
- Swelling of the ankles or abdomen.

In severe cases, bleeding from the gut or drowsiness and coma, can cause complications. The symptoms of liver disease due to alpha-1 antitrypsin deficiency in adults are similar to those in older children. But the disease may not become apparent for years. The symptoms are the same as with any other liver cirrhosis: jaundice, abdominal swelling, bleeding into the gut and, ultimately, coma.

DIAGNOSIS

- Family screening is usually done to see if there is a history in the family of similar problems.
- Many cases are probably never diagnosed. Alpha-1 antitrypsin deficiency is relatively easy to detect by testing the blood alpha-1 antitrypsin levels. The next step is to identify the exact genetic variant.
- A sample from the liver (*liver biopsy*) may be examined under the microscope by a specialist.
- Liver function should be checked and blood tests and further scans may be needed.

- Lung function can be measured by breathing tests, chest X-ray and CT scans.

TREATMENT

- Genetic counseling for affected families is recommended, as well as tests to identify relatives at risk.
- Finding out about a problem before a baby is born is possible, but may not be able to tell how bad the disease conditions will be.
- The standard treatment for emphysema is with inhaled medicines and antibiotics, which may be required to treat infections.
- Treatment (*therapy*) for cirrhosis and liver failure of any cause will be given.
- If conventional long-term treatment does not prevent continually worsening disease in the liver or lungs, organ transplantation may be considered.
- In end-stage emphysema, single lung transplantation is an option.
- Alpha-1 antitrypsin deficiency is the most common genetic disease requiring liver transplantation in children. But very few children with alpha-1 antitrypsin deficiency ever require a liver transplant. Those who do have a good outlook with 90 percent surviving one year, and 80 per cent surviving five years. Results in adults are not so good, possibly due to associated lung complications.
- Specific therapy for alpha-1 antitrypsin deficiency is difficult. Regular infusions of alpha-1 antitrypsin have been used. However, long-term benefit has not been seen.

PROGNOSIS

- The outlook for patients with alpha-1 antitrypsin deficiency is good.
- Many people are not aware that they have the condition.
- Liver or lung disease that keeps getting worse (*progressive*) affects only a small number of people affected, but can be serious. Regular monitoring is required.

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