Alpha 1 Antitrypsin Deficiency

PLAY PICMONIC

Characteristics

Decreased Alpha Anti Trypsin

Down-arrow Afro Ant-tie Trips-sun

Alpha 1 Antitrypsin Deficiency is characterized by decreased alpha antitrypsin. Alpha Anti Trypsin (AAT) is a protease inhibitor produced in the liver and used to prevent damage in the body from the neutrophil elastase enzyme secreted by white blood cells in infection. It protects 90% of the lower lungs from this protease (elastase) activity. The lack of protection from elastase in alpha antitrypsin deficiency will cause destruction in a site of the bodies that should be protected by alpha antitrypsin, especially the lower lungs.

Increased Elastase Activity

Up-arrow Elastic-pants-ace

The lack of inhibition of elastase in alpha antitrypsin deficiency will cause an increase in elastase activity.

Decreased Elastic Tissue

Down-arrow Elastic-tissues

The increased elastase activity in alpha antitrypsin deficiency will cause elastase's increased degradation activity, resulting in decreased elasticity of tissues. These will result in "toxic loss of function" in the lungs. On the other hand, "toxic gain of function" occurs in the liver due to the accumulation of unsecreted AAT protein.

Misfolded Protein Aggregates

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AAT deficiency occurs due to proteinopathy, which is a condition with abnormal synthesis, folding, post-translational modification, or accumulation of protein in cells or tissues. These will result in proteotoxicity and aggregation of misfolded protein, causing damaged cellular function.

PAS+ Globules

PEZ-Positive Globe

AAT deficiency can be diagnosed by the presence of PAS + (PAS-positive diastase-resistant) globules in the liver biopsy. Isoelectric focusing is the gold standard blood test for identifying AAT variants using phenotype characterization, such as MZ or ZZ.

Clinical Features

Panacinar Emphysema

Pan-ace M-fist-zebra

Clinical manifestation of AAT deficiency in the lungs will result in panacinar emphysema, which involves all portions of the acinus and secondary pulmonary lobule more or less uniformly. It is seen with expansion from the respiratory bronchiole to the alveoli. This is a characteristic of emphysema from AAT deficiency which differs from other emphysema, centriacinar emphysema. Smoking is strongly associated with centriacinar emphysema.

Dyspnea

Disc-P-lungs

The most common symptom of AAT deficiency is dyspnea, which can also accompany other pulmonary symptoms, including cough with sputum production and wheezing. This manifestation occurs due to the lack of protection in the lung from elastase activity.

Cirrhosis

C-roses-on-liver

The liver is the primary site of alpha antitrypsin production. Accumulation of misfolded proteins in AAT deficiency will induce fibrosis, resulting in cirrhosis.

Hepatocellular Carcinoma

Liver Car-gnome

Hepatocellular carcinoma can occur as a complication of alpha antitrypsin deficiency. The damage to the liver due to misfolded protein accumulations and Z allele mutation contributes to this process.