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Karthagener's Syndrome and Its Effects On The Respiratory Tract, Reproductive System and CNS

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Abstract:

Karthagener's syndrome, primary ciliary dyskinesia, hereditary disease of special ciliary cells, which was described by the Swiss doctor Manes Carthagener (1897 - 1975) in 1933. Carthagener's disease is a autosomal recessive genetic disease, two genes are involved in the process - DNAI1 and DNAH5, which mutation is caused by dynein underdevelopment and cilia movement defect.

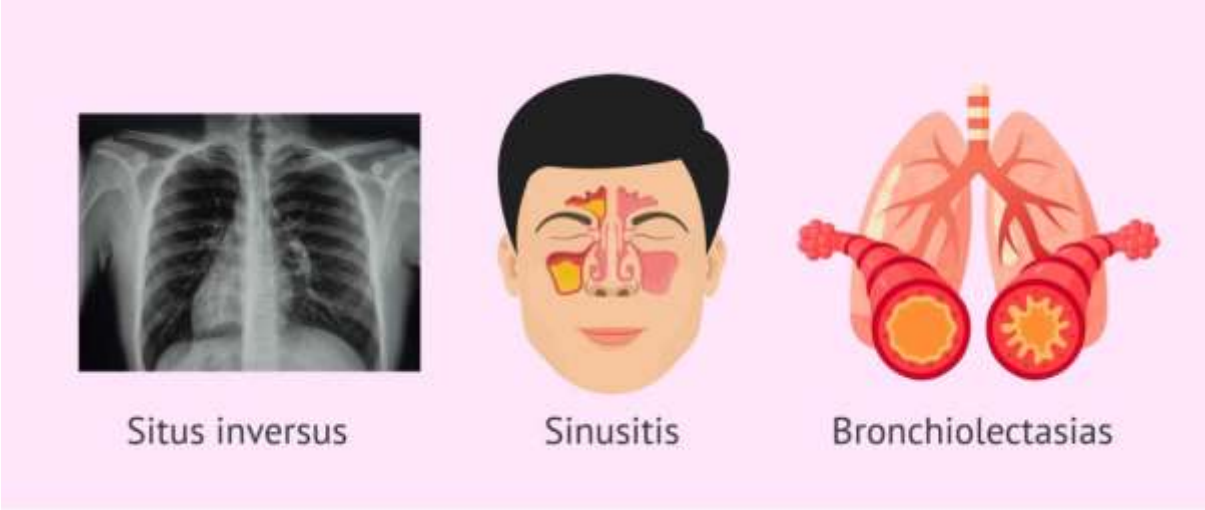
Human respiratory system includes the nose, sinuses, middle ear, Eustachian tubes, throat, and respiratory tubes (trachea, bronchi, and bronchioles). Respiratory tract is lined with special epithelial cells, which have cilium. Cilium usually act as a broom, that cleans the dust, smoke, toxins and bacteria inhaled by the body. Damaged ciliated component of the epithelial cell (it is caused by a defect of protein dynein) causes abnormal ciliary movement, followed by improper clearance of mucus from sinus cavities and bronchi, which in turn causes with various problems constantly or repeatedly sino-pulmonary infections. Cilium are also in the ventricles of the brain and the reproductive system. Patients suffering from the Karthagener's syndrome may experience headaches (intracranial hypertension may develop, due to insufficient movement of Cerebrospinal fluid(CSF)) and problems related to infertility (fallopian tubes are lined with cilium). Epidemiologically Karthagener syndrome occurs in approximately one in 32,000 newborns and it affects both gender. The syndrome does not depend on race and can occur at any age. The average life expectancy of humans with this syndrome is not determined. Life expectancy depends on how regularly and

effectively complications of the syndrome are treated. Especially cautious are the first 20 years. In cases of diligent care the duration of the life of patients suffering from Karthagener's syndrome is equal to the total statistical data. Most of the symptoms of the Karthagener's syndrome are due to delay of the function of cilia and there are different types.

Key words: Karthagener's syndrome, cilia, the respiratory system, the reproductive system, the central nervous system(CNS), etc.

Introduction

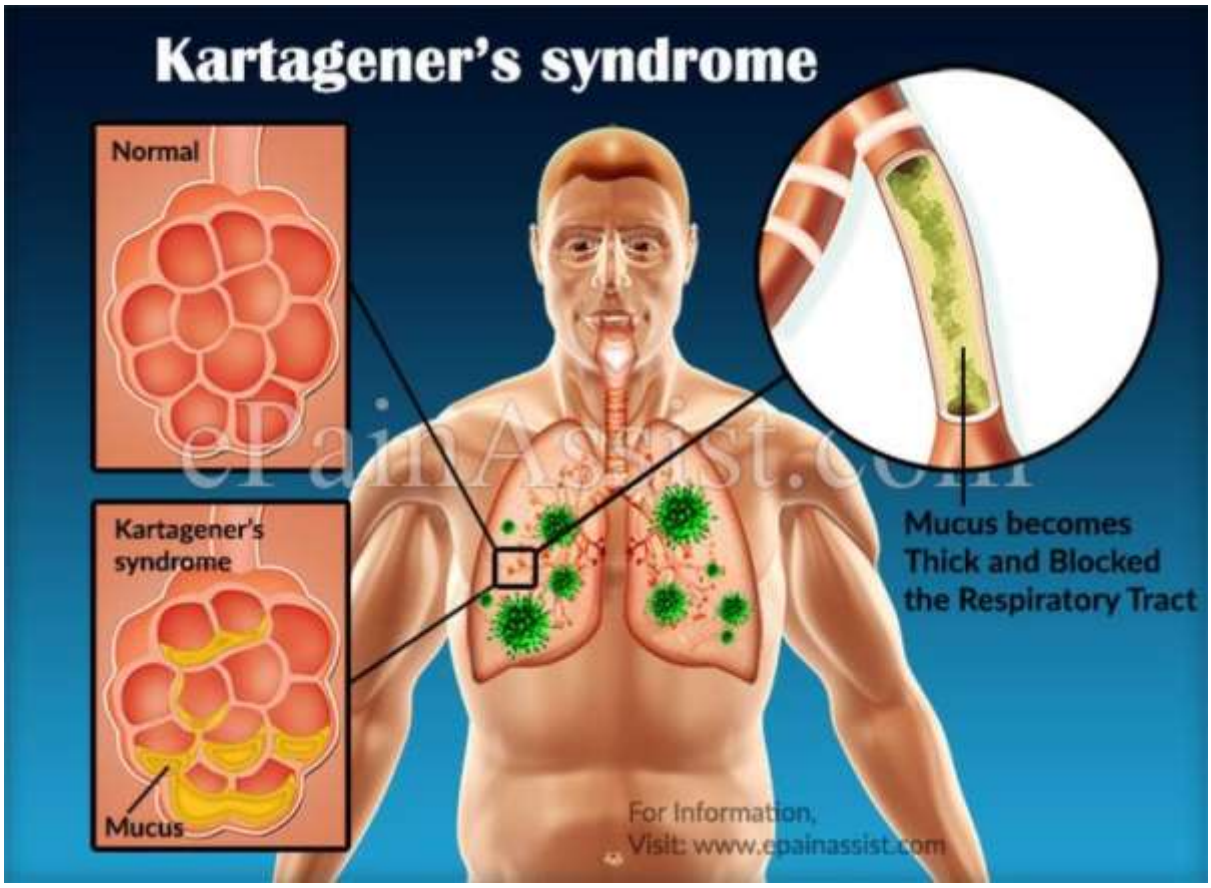
Imotile-cilia syndrome is rare, cilopathic, autosomal recessive genetic disorder that affects defect in the action of cilium in the airways and fallopian tubes. As a result, patients usually have chronic recurrent rhinosinusitis, otitis media, pneumonia and bronchiectasis caused by pseudomonal infection. When situs inversus (reverse location of internal organs), chronic sinusitis and bronchiectasis occur together, this is called Karthagener's syndrome. [3]



Some of the genes affected by Karthagener's syndrome are DNAI1, which is located on chromosome 9, DNAI1 on chromosome 7 and DNAH5 on chromosome 5. These genes encode elements of the protein dynein and they are responsible for the movement of cilium. Movement disorders can be congenital or acquired. Congenital disorders known as PCD (Primary ciliary dyskinesia). Almost 50% of PCD patients have situs inversus. PCD cases with situs inversus are known as Karthagener's syndrome. PCD is phenotypically and genetically heterogeneous condition, where the primary defect is in ultrastructure or function of the cilium or both. PCD is carried by 38% of patients with DNAI1 and DNAH5 mutations of dynein genes. [6]

The DNAH5 gene provides instructions for the synthesis of a protein that is part of a group (complex) of proteins called dynein. This complex functions in cell structures called cilia. Cilia are microscopic, finger-like projections that come out of the surface of the cells. Coordinated back and forth movement of cilium can move the cell or the fluid surrounding the cell. Dynein "produces" the force needed to move the cilia. In DNAH5 more than 80 mutations cause primary ciliary dyskinesia, which is characterized by respiratory tract infections, pathological placement of organs and childlessness. Mutations in the DNAH5 gene cause chain absence or deviation from the norm. Without the normal version of this subsection, the ODA (outer shoulder of dynein) cannot be formed properly and may

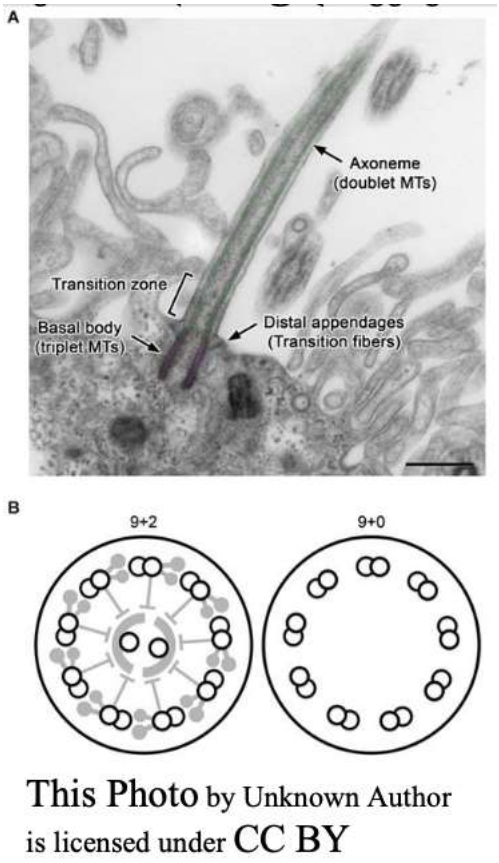
be reduced or absent altogether. As a result, cilium cannot form the force required for forward and backward movement. Defective cilium cause features of primary ciliary dyskinesia. [7] [8]



As for the direct effect of Karthagener's syndrome on the respiratory, reproductive and nervous systems - manifests itself in the form of several diseases. Unmistakable confirmation of the Karthagener's syndrome is done by biopsy. They take the material from the surface of the cavity of the tracheal lung sinus and by means of a microscope they determine the presence of defective cilium. 100% diagnosis of this syndrome can be diagnosed with a genetic test, by confirming the mutation of the above mentioned genes.

Complications of Carthagener syndrome include:

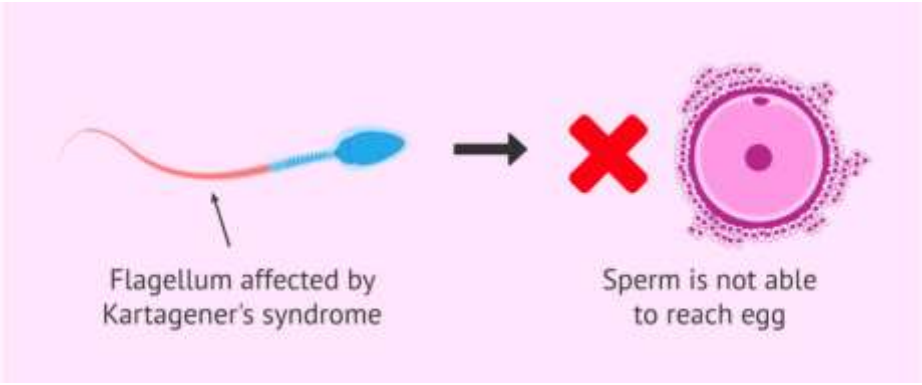
- Chronic sinusitis, otitis, rhinitis;
- Chronic pneumonia;
- Follicular bronchiectasis (degeneration of bronchi);
- Conductive deafness;
- Hydrocephalus;
- Nasal polyps;
- Infertility.



Case – Report - Respiratory System

A 24-year-old man from the city of Gondar (north-west Ethiopia) applied Gondar University Hospital - with cases of Recurrence of Nasal Edema, itching, paranasal discomfort and productive coughing for more than a decade. Clinical and Imaging findings revealed chronic sinusitis, bronchiectasis, dextrocardia and situs inversus. He was treated with oral Antibiotics, mucolytics and chest physiotherapy. With the above mentioned therapy he was symptomatically better and started long-term low-dose prophylactic antibiotic administration.[9]

Impaired function of cilium movement in specific areas causes chronic recurrent respiratory diseases of the paranasal sinuses and respiratory tract infections and infertility. Movement of cilia during embryogenesis results in left-right lateral defects, such as Situs Solitus (only dextrocardia) or Situs Inversus Totalis, where transpositions of thoracic and abdominal organs are observed. [9]



Karthagener's syndrome can cause infertility in all genders. In men, spermatozoon flagella- also known as "motile tails" - can be directly affected and because of this it loses ability to move. In women, it causes the lining of the fallopian tubes violation of cilia mobility, which hinders or prevents it altogether moving the egg. This condition is one of the causes of childlessness. [10]

Hydrocephalus is a neurological disorder caused by abnormal accumulation of cerebrospinal fluid deep in the brain in the ventricles. This excess fluid causes the ventricles to dilate, creating harmful pressure affects brain tissues. Hydrocephalus can be detected after birth or shortly after, or it can happen over time as a result of damage.

Cerebrospinal fluid (CSF) is an ultrafiltrate of plasma contained within the ventricles of the brain and the subarachnoid spaces of the cranium and spine. It performs vital functions, including providing nourishment, waste removal, and protection to the brain. It "feeds" the brain and spinal cord until it is absorbed into the bloodstream. The rule is to produce enough CSF each day and absorb the same amount. Excessive accumulation of CSF can interfere with the brain function properly and cause brain damage or even death.[11]

Conclusion

Therefore, a fragment as small as cilia, in the human body, can the aforementioned (and not only) vital causing significant change. In countries like the USA, Israel and Germany, the life of patients with this diagnosis become extended. Unfortunately, the result in the most countries is lethal.

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