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EARLY DIAGNOSIS AND TREATMENT IN PATIENT WITH A PRIMARY CILIARY DYSKINESIA (KARTAGENER SYNDROME): CASE REPORT

Abstract

Primary ciliary dyskinesia is an orphan disease known for its multiple and variable symptoms caused by its genetic heterogenity. Frequent inflammatory diseases of both upper and lower respiratory tract are key symptoms in children. Kartagener syndrome is a classical form of the primary ciliary dyskinesia, which includes such symptoms as situs inversus, bronchoectasis, and hypoplasia of paranasal sinuses and/or sinusitis. According to some foreign research, the median age of primary ciliary dyskenesia diagnosis in Eastern and Western European is about 5 years old. Lack of early diagnosis is nothing but a direct consequence of the poor level of awareness, which is common for a primary health care system. This itself leads to increased rates of patients disability. This report deals with clinical, diagnosis and treatment peculiarities of a primary ciliary dyskinesia (Kartagener syndrome) patient. Both mother's tough obstetric-gynecological profile and a harsh course of this particular pregnancy were taken into account. Numerous respiratory infections in this patient were treated on an out-patient basis up to 11 months. Kartagener syndrome was diagnosed at our clinic based on laboratory and instrumental tests results. Complete situs inversus was revealed.. The diagnosis was confirmed by histomorphological patterns revealed in the nasal epithelial biopsy specimen. A difficulty to come up with the Kartagener syndrome diagnosis at the out-patient care stage is in focus of this specific case report. Noteworthy, we have succeeded in early diagnosis of Kartagener syndrome and then in a following effictive therapy conducted in our clinic.

Key words: *primary ciliary dyskinesia, Kartagener syndrome*

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PCD — primary ciliary dyskinesia

Introduction

Primary ciliary dyskinesia (PCD) is a genetically determined disease underlain by congenital defects of epithelial motile cilia in respiratory tract and similar structures leading to disruption of cilia motility [1, 2]. This is a relatively rare disorder with an incidence rate of 1:30 000 to 1:50 000 newborns [3]. Late diagnostics and PCD treatment inevitably lead to early disability.

The most common and classic form of PCD is Kartagener syndrome (situs inversus, chronic bronchiectasis, hypoplasia of paranasal sinuses or sinusitis). This form comprises 50–60% of cases [2].

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There have been several attempts to decode bronchiectasis genesis in subjects with situs inversus. Defects in prenatal development were proposed as a cause of this syndrome. However, the true nature of bronchopulmonary disorder in Kartagener syndrome was revealed only in the 70's, when R. Eliasson and B. Afzelius found a defect in cilia axonemes in the ciliated epithelium of the respiratory tract mucosa. In vitro studies showed that ultrastructural defects do not always lead to complete immobility of cilia. Rather, they only affect the activity of their beating, which becomes slow and chaotic [4, 5].

Genetically determined ultrastructural defect is common, since ciliated epithelium lines not only the respiratory tract, but also the organ of Corti, sperm flagella, ciliated cells of cerebral ventricles ependyma, photoreceptors of the retina, ciliated cells lining biliary ducts, renal tubules, and Fallopian tubes.

In addition, there are cilia on the primitive knot that ensure rotation of internal organs during prenatal development; therefore, half of the patients have situs inversus [6, 7].

It is commonly believed that PCD is an autosomal recessive disorder. However, we cannot exclude that defects of cilia can result from a new mutation [2].

According to foreign studies, the median age of PCD diagnosis in Western and Eastern Europe is 5.3 years; however, in case of situs inversus it is diagnosed earlier (at the median age of 3.5 years), than with normal organ position (5.8 years) [8].

In Russia, the median age of PCD diagnosis in children with situs inversus is approximately the same as in Europe — 4 years, while without situs inversus PCD is diagnosed later (at the median age of 7.6 years) [9].

When the disease follows a classic course of development, labored nasal breathing (snuffles), purulent discharge from the nose, frequent otitis, repeated bronchitis and pneumonia are observed during the first days of life. Later purulent or mucopurulent endobronchitis develops, followed by circumscribed pneumosclerosis with bronchi deformation. It can lead to bronchiectasis. Impairment of reproductive function is registered in adults (in men — decreased sperm motility, oligospermia, infertility; in women — ectopic pregnancy and infertility) [1].

Treatment is symptomatic. The main focus is on anti-inflammatory therapy and maintenance of bronchial drainage function (postural drainage, inhalations, transnasal bronchial drainage, sinuses lavage, chest massage, physiotherapy). If a chronic respiratory infection becomes aggravated, antibiotics are used [10].

Prognosis depends on the severity of bronchopulmonary process. In cases of localized bronchiectasis with no respiratory failure, early diagnosis and prompt treatment, the recovery rate is favorable. In cases of advanced pulmonary process, respiratory failure develops relatively quickly, cor pulmonale is formed, septic intoxication is pronounced, and growth retardation, i.e., disability, is observed. Some patients die at an early age [2].

Case report

An 11-year old boy, T., is observed and treated in the Children's Hospital with the following principal diagnosis: congenital lung and heart abnormality. Primary ciliary dyskinesia (Kartagener syndrome): situs viscerum inversus. Chronic obstructive bronchitis, continuously recurrent course. Bilateral chronic maxilloethmoidal sinusitis, continuously recurrent course. Bilateral chronic secretory otitis. Bilateral conductive hearing loss.

Secondary diagnosis: Atopic dermatitis, pediatric form. Minor cardiac development abnormalities: multiple chordae tendineae of the left ventricle. Chronic gastroduodenitis. Hypotonic biliary dyskinesia. Dysmetabolic nephropathy. Grade 1 thoracic scoliosis.

It was a third pregnancy (the first and second ones resulted in fetal death at week 12–13). The course of the present pregnancy was complicated by an appendectomy at week 12, shingles at week 17, and threatened miscarriage at weeks 27–28. The delivery was at term. The newborn was of normal weight and height. The parents divorced after this pregnancy. Data on history of chronic diseases of the father are absent. The mother had no family history of this disease.

Since the age of 3 months the child had periodic cough and recurrent obstructive syndrome with predominantly passive mechanism (thick purulent sputum). The child was observed by a primary care pediatrician and received symptomatic

treatment. However, no instrumental diagnostics were performed. At the age of 11 months, the child was first admitted to our department, where we diagnosed the following based on examination data: primary ciliary dyskinesia (complete Kartagener syndrome). Comprehensive treatment was performed. At the age of 1 year, the child was diagnosed with chronic sinusitis and adenoiditis, with several relapses per year. Starting at age 2, the child had recurrent atopic dermatitis, which was exacerbated by cow milk and soy products intake. Starting at age 4 he had periodic abdominal pains. Diagnosis: hypotonic biliary dyskinesia. At the same time (starting at age 4) the child was diagnosed with chronic maxilloethmoidal sinusitis, and starting at age 7 he was diagnosed with bilateral recurrent otitis with conductive hearing loss. The patient underwent multiple examinations, was treated at an ear, nose and throat clinic, and received adenoidectomy. Relapses of bronchial obstruction were observed almost every month, with exacerbation of chronic bronchitis. He had pneumonia 6 times. Lung CT was performed twice: dextrocardia with right-side aortic arch and left-side superior vena cava, increased parahilar bronchovascular markings, roots are poorly structured due to vascular component and moderately dilated. A chest X-ray is presented in Figure 1.

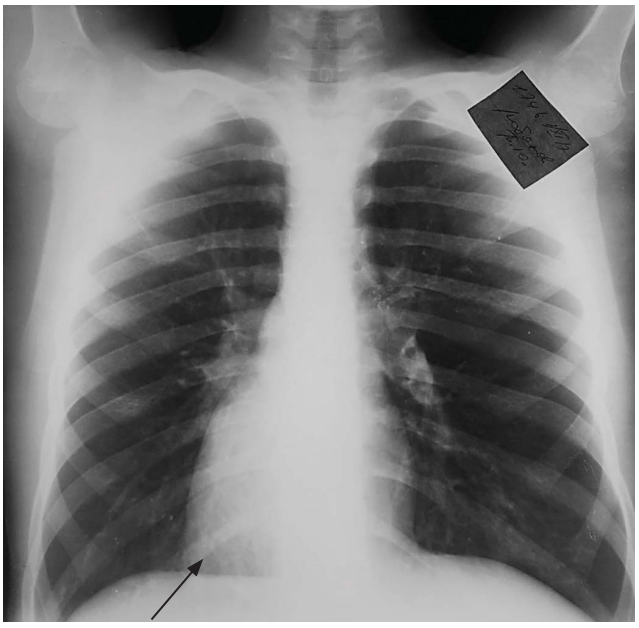

Figure 1. *Chest X-ray. The heart is shifted to the right. Increased pulmonary vascularity in hilar area*

In June 2017, the child was examined and treated at the Veltischev Research and Clinical Institute for Pediatrics (Moscow, Russia) with the following diagnosis: congenital bronchopulmonary abnormality: Kartagener syndrome, exacerbation of chronic bronchitis. Biopsy specimen of ciliated epithelium from nasal mucosa was analyzed. Conclusion: the child suffered from pronounced impairment of the ciliary function of the epithelium. There was evidence of primary ciliary dyskinesia.

Examination results: skin and visible mucosa were pale, clean, and moderately moisturized. Nasal breathing was difficult, and there was no discharge. There was no hyperemia of the oral pharynx. The tongue was moistened, white-coated at the root. The chest was normosthenic. Respiratory activity was symmetrical bilaterally. Bandbox resonance was observed. Harsh respiration without rales was auscultated. The patient had a productive cough with difficult expectoration. The cardiac area lacked any visible abnormalities. The following boundaries of relative cardiac dullness were observed: right — 1 cm to the outside of the right midclavicular line in the fifth intercostal space; upper — along the second intercostal space; and left — along the left edge of the sternum. Heart tones were clear, regular, with systolic noise centered in the apex and Erb's point. The abdomen was soft in palpation, with tenderness in the left hypochondrium and epigastrium. The liver was 0.5 cm below the left costal margin. Costovertebral angle tenderness was negative. The patient urinated without obstruction. The stool was formed and regular.

The child is continuously examined and treated in our clinic. He undergoes courses of anti-relapse therapy three times per year. This includes methods that improve bronchial function: drainage massage and postural drainage. The child is trained to do respiratory exercise. Treatment included inhalations with mucolytics and bronchospasmolytics. Antibacterial therapy is indicated based on microflora susceptibility to medications, including reserve antibiotics as needed. To prevent bronchiectasis and symptoms of descending infection as well as to reduce the frequency of exacerbations, the child received immunomodulatory treatment with intravenous immunoglobulins.

Due to timely and adequate conservative treatment, the state of this patient today has improved significantly with decreased symptoms of the disease.

Conclusion

Therefore, this case demonstrates the difficulties of diagnosing Kartagener syndrome at the outpatient stage, which can be related to the rareness of the disease and insufficient knowledge of the healthcare personnel. Early diagnosis (before the age of 1 year) in a hospital and promptly initiated treatment made it possible to minimize the development of complications.

If children have frequent relapses of respiratory tract infections, they should undergo chest X-ray to diagnose Kartagener syndrome in a timely fashion.

Conflict of interests

The authors declare no conflict of interests.

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