A case of Kartagener syndrome in the newborn

Kartagener syndrome is a rare autosomal genetic disease, accounting for approximately 50-60% of the cases of primary ciliary dyskinesia and characterized by the clinical trial of chronic sinusitis, bronchiectasis and situs inversus. We present a case report about a newborn baby with tachypnoea, retraction, rales and dextrocardia. The demonstrated clinical case confirms the necessity of detailed examination of newborns with respiratory disorders, with the purpose to detect the congenital bronchopulmonary pathology. The immotile cilia syndrome should be added to the list of causes of respiratory distress in newborn infants. Genetic study, as well as electron microscopy of the biopsy of the mucous membrane of the nose or bronchi, for the determination of the mobility of cilia in a phase contrast microscope, is recommended for verifying the diagnosis of Kartagener syndrome.

Keywords: ciliary dyskinesia, Kartagener syndrome, newborns, situs inversus

Introduction

Primary ciliary dyskinesia (PCD) is a rare genetically and phenotypically heterogeneous hereditary disorder mainly transmitted by autosomal recessive inheritance and characterized by bronchiectasis, sinusitis and otitis media(1). The coexistence of PCD and situs inversus is known as Kartagener syndrome (KS) and it occurs in 50% of PCD cases(2). Kartagener syndrome develops as a direct result of congenital defect in motile cilia covering the respiratory epithelium, leading to mucociliary clearance deterioration and, thus, to clinical manifestations, such as respiratory distress in neonates, recurrent respiratory tract infections, bronchiectasis, situs inversus, infertility and heterotaxy(3). The true incidence is unknown, but it is estimated to affect 1:20,000 to 1:100,000 of live births (4). The severity differs from one patient to another, even among siblings, and it has rarely been recognized among infants. Thus, early diagnosis and management of this pathology are important and might help prevent irreversible lung lesions and forestall chronic lifelong sequelae.

Hereby, we report a case of situs inversus and respiratory distress syndrome in a neonate.

Case report

This female baby of Caucasian race was born after the second full-term pregnancy (39 weeks of gestation). The pregnancy was complicated by mild anemia and acute respiratory viral infection. The baby was born by normal vaginal delivery with a birth weight of 2800 g (50th percentile), Apgar score of 8 (at 1 minute of life and at 10 minutes of life).

Few hours after birth, she developed signs of respiratory distress, with rhinitis, nasal flaring and mild retractions for which she was transferred to the Neonatal Department of Children’s Regional Clinical Hospital on the third day of life for further diagnosis and management. With further investigations and detailed family history anamnesis, it was revealed that the first child (a 7-year-old girl) had a history of recurrent sinusitis with recurrent upper respiratory infections (bronchitis).

On admission, the physical examination revealed moderate respiratory distress characterized by dyspnea, with moderate intercostal and subcostal retractions, nasal obstruction (due to abundant mucus secretions) and perioral cyanosis. Breathing was rhythmic, with a respiratory rate of 60 breaths/minute. The heart rate was normal, at 150 beats/minute. Lung percussion showed hyperresonant breath sounds over the lateral lung fields and dullness at the lower posterior parts of the lungs. Weakened breath sounds and bilateral bubbling rales were revealed at lung auscultation. The heart sounds were best heard on the right of the sternum, leading to the clinical suspicion of dextrocardia. Chest X-ray revealed dextrocardia, increased bronchovascular markings, peribronchial infiltration and marked bilateral hyperinflation (Figure 1).

The abdominal ultrasound confirmed the diagnosis of total situs inversus, with no other malformations revealed. Cardiac ultrasound was done, showing the typical pattern of mirror image dextrocardia with a normal ECG. To note, laboratory findings showed normal white cell-count, with normal C-reactive protein.
However, the parents’ consent could not be obtained in order to carry out the diagnostic bronchoscopy with biopsy of the respiratory mucosa. In addition, bronchography was postponed because of the low probability of early-onset bronchiectasis.

Thus, Kartagener syndrome was confirmed based on the clinical and imaging findings. The treatment with bronchodilators and antibiotics was initiated immediately after birth, with intensive respiratory physiotherapy prescribed. The patient’s respiratory distress greatly ameliorated and she was discharged home without any pathological clinical signs on the 14th day of life. Recommendations of regular follow-up, and referral to specialized PCD diagnostic and treatment center were given before discharge.

The follow-up of the patient at the age of 3 months showed the presence of recurrent respiratory episode with signs of rhinitis, bronchitis and fever, for which she was treated with antibiotics and inhaled bronchodilators.

**Discussion**

Primary ciliary dyskinesia belongs to a relatively small group of genetic disorders that carries an autosomal recessive type of inheritance\(^5\). The first report of PCD was published by Siewert in 1904, after which Kartagener, in 1933, was the first to describe the PCD syndrome as a triad of situs inversus, bronchiectasis and recurrent sinusitis, for which it bears his name, the Kartagener syndrome (KS)\(^6\). In 1980, Sleigh together with 23 other researchers considered that the name PCD should only be used in case of congenital ciliary disorders, while “secondary ciliary dyskinesia” should be used with acquired ciliary diseases\(^8\).

Normal ciliary function is extremely important in respiratory host defense. Its impairment causes the typical signs and symptoms of chronic sinusitis and chronic bronchitis, that eventually lead to bronchiectasis\(^9\). The lower respiratory tract, from the trachea to the respiratory bronchioles, contains ciliated cells which consist of approximately 200 cilia that vary in length from 5 to 6 μm and decrease in size as the airway becomes smaller. They are composed of central axonemes containing 9 pairs of microtubules that have an outer and inner dynein arms and form a circle around two central microtubules. The most common abnormalities in patients with primary ciliary dyskinesia are the absence of dynein arms, radial spokes or microtubules. They lead to a wide range of defects in ciliary ultrastructure and motility, which ultimately impairs ciliary beating and mucociliary clearance. About 50% of these patients have situs inversus totalis, with the transposition of the thoracic and abdominal organs (Kartagener syndrome). This malformation appears due to the disorders of cilia that in normal condition facilitate the correct orientation of viscera sinus in the embryo\(^11\).

The early diagnosis is beneficial in KS patients; however, it is well known that this pathology is usually missed in the neonatal period because only 50% of patients with immotile cilia syndrome show situs inversus. On the other hand, sinuses are undeveloped in infants and bronchiectasis and lung function decrements typically start at preschool period. In addition, symptoms that are typical for this disease (cough, rhinitis and otitis) are common for various pathologies of infancy\(^19\). That is why the diagnosis is often delayed until late childhood or adulthood as a consequence of the heterogeneous nature of the disease, the lack of physicians’ knowledge, and the technical difficulties required for an accurate diagnosis\(^4\).

Recently, only several clinical presentations confirmed PCD in neonates with respiratory distress and unexplained cough, in combination with dextrocardia. Hugo Alejandro Vega Ortega et al. showed six cases of Kartagener’s syndrome manifested by the association of sinusitis, situs inversus and bronchiectasis of which respiratory symptoms began in infancy in only three patients\(^15\). Andrew Whitelaw et al. also reported six patients who had signs of both lower and upper respiratory tract disorders within the first 24 hours of life, of which five of them had situs inversus\(^16\). On the other hand, Tara Mullowney et al. reviewed 51 cases of PCD from 1994 to 2012 with a documented history of neonatal respiratory disorders (transient tachypnea of the newborn, neonatal pneumonia, meconium aspiration, pneumothorax and others), need for oxygen therapy and respiratory support (mechanical ventilation or continuous positive airway pressure), situs status (situs solitus, situs inversus), documented ciliary defect (outer dynein arm, inner dynein arm, central apparatus or in-determinate) and genetic test results confirmation\(^17\). Ciancio
et al. reported about seven neonates with confirmed KS from 2006 to 2014 which manifested with tachypnea, hypoxemia or even respiratory failure requiring mechanical ventilation and *situs inversus* (18).

The received results suggest that a diagnostic work-up for primary ciliary dyskinesia should be considered in a term infant, usually born after an uncomplicated pregnancy, with simple delivery, and unexplained respiratory disorders, that sometimes require prolonged oxygen therapy, with dextrocardia. Any combination of these findings requires a referral to a pediatric pulmonologist to provide complex diagnostic work-up with further confirmation of KS.

The diagnostic approach to PCD is evolving (19,20). Until recently, the electron microscopy has been considered a gold standard to define ultrastructural defects in cilia demonstrating obvious ciliary dysfunction (immotile or profoundly dyskinetic cilia) (21). Emerging diagnostic tests include genetic testing, nasal NO measurement, immunofluorescent analysis and high-speed videomicroscopy (22-24). These specialized diagnostic tests are not readily available; therefore, referral to research centers may be needed.

In our patient, KS was suspected because of respiratory disorders that have manifested after delivery and *situs inversus totalis*. We have not found any other reasons for respiratory distress and that is why we suspected that the primary ciliary defect caused the respiratory problems. However, the demonstration of abnormal ciliary movement needs electron microscopic studies of biopsies obtained from the nasal mucosa or trachea. However, these procedures are invasive and available only at specialized centers; therefore, the diagnosis of Kartagener’s syndrome in this case was clinical, supported by imaging studies.

There is a lack of evidence-based medicine in the management of Kartagener syndrome (25). The treatment of this pathology is mainly based on the prevention of recurrent infections that might worsen bronchiectasis, resulting in a more rapid lung function decline, and this is often the reason for their morbidity. Thus, the goals of respiratory management are the improvement of lung function and the limitation of disease progression, and they are based upon airway clearance enhancement and antibiotic therapy (26). KS patients are frequently troubled by repeated infection episodes for which they have to seek medical attention. Regular physiotherapy and correct antibiotic treatment of respiratory infection offer the best way of preventing irreversible pulmonary lesions (27).

Conclusions

Although the classic triad of symptoms may not be present in the neonatal period, the diagnosis of Kartagener syndrome or PCD should be considered in an infant with unexplained respiratory distress, especially when *situs inversus* is present. A non-invasive screening can be used for its early detection. Electronic microscopy, genetic counseling, and social and psychological support in specialized centers should be recommended. Early diagnosis and the treatment of associated complications of this rare syndrome significantly improve the quality of life and the prognosis of patients.

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References