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Kartagener syndrome – a very rare cause of neonatal respiratory distress

Rebeka Ribičić[1], Jesenka Borošak[1], Tomislav Baudoin[1], Stela Bulimbašić[2], Tomislav Ribičić[3], Iva Mihatov Štefanović[1], Jasna Tumbri[1], Lorita Mihovilović Prajz[1]

We report on a newborn with respiratory distress and situs viscerum inversus totalis. Kartagener syndrome was suspected because of respiratory distress, oxygen dependence, atelectasis, thick nasal mucus, productive cough and situs viscerum totalis. The diagnosis of primary ciliary dyskinesia was confirmed by electron microscopy. We suggest that, despite its rarity, primary ciliary dyskinesia should be considered in any newborn with unexplained respiratory distress. Also, we emphasize the diagnostic role of thick nasal mucus and productive cough, both very rarely seen in neonates. Early diagnosis of primary ciliary dyskinesia may allow for early initiation of physiotherapy and multidisciplinary care, in order to preserve lung function in this genetic disease as long as possible. To our knowledge, this is the first report of Kartagener syndrome diagnosed in a newborn in Croatia.

Keywords: infant, newborn; Kartagener syndrome; respiratory distress syndrome, newborn

INTRODUCTION

Our patient, a term infant, was diagnosed with Kartagener syndrome in the early neonatal period following presentation with unexplained respiratory distress and *situs viscerum inversus*. This allowed for early initiation of physiotherapy and multidisciplinary treatment and follow up.

CASE REPORT

A 3.56-kg term male infant was born by cesarean section to a 24-year-old gravida 2 para 1 mother. Prenatal screens were unremarkable. Apgar scores were 10 and 10 at 1 and 5 minutes, respectively. In the very first hours of life, the newborn was noted to have nasal congestion, cough and tachypnea, increasing his work of breathing within hours. He was admitted to the neonatal intensive care unit. White cell count was normal, C-reactive protein slightly elevated (24.9 mg/L), blood cultures and nasopharyngeal aspirate were negative. Chest radiograph revealed atelectasis at the right middle lobe and dextrocardia. Echocardiogram revealed dextrocardia with open foramen ovale. Abdominal sonography confirmed *situs viscerum inversus*. Antibiotics were started and administered for 5 days. He continued to have respiratory distress and required oxygen during the first 8 days. Until the day of discharge (postnatal day 22), he continued to have thick nasal mucus with cough, so he required frequent nasal discharge, saline inhalations and chest physiotherapy. Nasal ciliary biopsy was also performed. Electron microscopy of the nasal cilia demonstrated qualitative and quantitative abnormalities of kinocilia, suggesting primary ciliary dyskinesia: normal 9+2 arrangement of the microtubules but with a reduced number of the outer and inner dynein arms, shorter cilia and abnormal ciliary orientation. Prior to discharge, multidisciplinary follow up was arranged.

DISCUSSION

Kartagener syndrome (KS) is a rare heterogeneous autosomal recessive disease. The prevalence of KS is 1 case *per* 32,000 live births (1). KS is a type of primary ciliary dyskinesia (PCD) associated with *situs viscerum inversus*. PCD can result from mutations in many different genes.

Although much progress in gene identification for PCD has been achieved, it has been recently estimated that the

[1] CHC "Sestre milosrdnice", Vinogradska 29, 10000 Zagreb
[2] CH Dubrava, Avenija Gojka Šuška 6, 10000 Zagreb
[3] Children's Hospital Zagreb, Klaićeva 16, 10000 Zagreb

Correspondence to:
Rebeka Ribičić, MD, CHC "Sestre milosrdnice", Vinogradska 29, 10000 Zagreb, e-mail: rebeka2809@gmail.com

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known genes in which mutations cause PCD account for about 65% of PCD cases. Mutations in the *DNAI1* and *DNAH5* genes account for up to 30% of all PCD cases (2).

In an attempt to identify additional PCD causing mutations, one of the newest studies by *Hjeij et al.* revealed loss-of-function mutations in *CCDC151* in three unrelated families characterized by PCD with specific loss of the outer dynein arms and severely impaired ciliary beating (3). In many cases of PCD, the cause of the disorder is unknown. Mutations in the genes that cause PCD result in defective cilia that move abnormally or are immotile. Defective embryonal monocilia are thought to cause random organ rotation during embryonal period. As a result, approximately 50% of PCD patients have *situs inversus*, and the other half of PCD patients have normal *situs viscerum*. Symptoms of PCD may start in early childhood and the mean age at diagnosis is 4.4 years (4). However, the diagnosis is often missed and symptomatic treatment for recurrent upper and lower respiratory tract infections is offered in most cases. A history of onset of respiratory symptoms in the neonatal period in children with chronic respiratory problems is strongly suggestive of PCD. Seventy-six percent of those children have neonatal history of persistent rhinitis, 67% neonatal respiratory distress and 69% *situs inversus* (4). Approximately 12% of affected children have complex congenital heart disease. Because of impaired mucociliary clearance, infants with PCD have a major risk of recurrent, chronic infections of the lungs, middle ear and paranasal sinuses. Also, male infertility and defects in neutrophil chemotaxis can be present (5). Ciliated epithelium covers most areas of the upper and lower respiratory tract, reproductive organs and ependyma. The typical ciliary axoneme consists of 2 central microtubules surrounded by 9 microtubular doublets comprised of an A and a B subunit. There are several proteins described (nexin as most important) that interconnect the outer doublets to each other, and the inner and outer dynein arms. Each A subunit is attached do 2 dynein arms that contain adenosine triphosphate (ATP). The basic mechanism for ciliary motion is mediated by dynein arm of one A subunit that is attached to the dynein arm of the adjacent B subunit. ATP is hydrolyzed by the dynein arms and 9 microtubule doublets as they slide against each other. Patients with PCD have a wide range of defects in ciliary ultrastructure and motility, which ultimately impairs ciliary beating and mucociliary clearance. The most common defect is reduction in the number of dynein arms (over 95% of cases), but absent radial spokes and central tubules, transposed doublets, abnormal basal cell apparatus, cilia with abnormal length and normal ciliary ultrastructure with abnormal arrangement and beat direction can also be found (6). Diagnostic tests include imaging studies, saccharine and nitric oxide tests, pulmonary function studies, but the only standardized definitive diagnostic test to visualize ciliary ultrastructure is nasal mucosa brushing or biopsy and bronchial mucosa biopsy, which are obtained for electron microscopy, (7).

The classic PCD symptoms may not be present in the neonatal period, but neonatologist should consider the diagnosis of PCD or KS in a newborn with prolonged or recurrent or unexplained respiratory distress or pneumonia, oxygen dependence, atelectasis, thick nasal mucus and productive cough, especially *when situs inversus totalis* is present. It is very important to make the diagnosis as early as possible, as regular physiotherapy and postural drainage may prevent recurrent respiratory infections and progression to bronchiectasis.

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SAŽETAK

Kartagenerov sindrom- vrlo rijedak uzrok novorođenačkog distres sindroma

R. Ribičić, J. Borošak, T. Baudoin, S. Bulimbašić, T. Ribičić, I. Mihatov Štefanović, J. Tumbri, L. Mihovilović Prajz

U našem radu opisujemo novorođenče s respiratornim distresom udruženim sa situs viscerum inversusom. Na Kartagenerov sindrom posumnjalo se zbog respiratornog distresa, ovisnosti o kisiku, atelektaze, gustog nosnog sekreta, produktivnog kašlja i potpunog situs viscerum inversusa. Dijagnoza primarne cilijarne diskinezije potvrđena je elektronskom mikroskopijom. Naša sugestija je da treba razmotriti postojanje primarne cilijarne diskinezije, unatoč njenoj rijetkosti, u svakog novorođenčeta s neobjašnjivim respiratornim distresom. Također želimo naglasiti dijagnostičku važnost gustog nosnog sekreta i produktivnog kašlja, koje oboje vrlo rijetko viđamo u novorođenčadi. Rano postavljena dijagnoza PCD-a bitan je korak u ranom započinjanju fizikalne terapije kao i potrebne multidisciplinske skrbi, što osigurava očuvanje što duže plućne funkcije u ove genske bolesti. Prema našim spoznajama, ovo je prvi opisani slučaj novorođenčeta s potvrđenom dijagnozom Kartagenerovog sindroma u Hrvatskoj.

Ključne riječi: novorođenče; Kartagenerov sindrom; respiratorni distres