Neonatal Diagnosis of the Immotile Cilia Syndrome*

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The immotile cilia syndrome is an inherited disorder characterized by inappropriate motility of the cilia. The clinical symptoms include recurrent sinopulmonary infections and reduced fertility. In about half of the cases, situs inversus is encountered. The case presented is that of a two-day-old boy in whom diagnosis was based on ultrastructural abnormalities. Early diagnosis permitted immediate symptomatic treatment and an absence of infections during a 37-month period of observation. Nasal biopsies performed in six newborns with various degrees of respiratory distress secondary to classic neonatal respiratory problems and in a healthy one-day-old newborn demonstrated the presence of normal ciliary structures at birth. In cases without situs inversus, diagnosis of the immotile cilia syndrome may be difficult. The importance of early diagnosis and management is stressed; the ultrastructural abnormalities are present at birth in newborns with the immotile cilia syndrome.

The immotile cilia syndrome is a disorder characterized by inappropriate motility of the cilia in the airways and other ciliated organs. It is a congenital disease, probably recessively inherited. The clinical symptoms include recurrent episodes of bronchitis, sinusitis, nasal polyposis, otitis, mastoiditis, and reduced fertility. In about half of the cases, situs inversus is encountered.

The symptoms are a result of abnormal morphology of the cilia, the dynein arms normally attached to nine microtubular doublets which provide normal ciliary movement are absent; this causes an inability to beat and a reduced clearance of mucus and particles, resulting in chronic infections.

The case presented is that of a newborn in whom the full entity, including ciliary defects, is documented on the third day of life. Normal ciliary structure could be found in six newborns with other causes of respiratory distress and in a normal newborn.

Case Report

A male child was born to a healthy 33-year-old woman following a normal pregnancy. There was no prenatal or postnatal asphyxia; the Apgar scores were nine and ten. The birth weight was 2,650 g. Two days after delivery, the child developed some respiratory difficulties, including tachypnea and retractions. Auscultation was reported as particularly clear in the right hemithorax. The chest x-ray film revealed dextrocardia, while the pulmonary fields were clear. Repetitive chest x-ray films remained unchanged; no radiologic signs of neonatal pulmonary diseases appeared. Bacteriologic investigations, including cultures of blood, urine, nasal secretion, and throat swabs, were negative. The results of the sweat test were normal. The lecithin/sphingomyelin ratio on gastric aspirate was normal. The IgE level was 1.0 kilounits/L. The level of α1-antitrypsin was 223 mg/100 ml (normal range). The localization of liver, spleen, and colon studied by ultrasound and opacification confirmed that the child had situs inversus totalis. Bronchoscopy confirmed the reversal of visceral status and the presence of very thick secretions.

On the third day the infant still had persistent symptoms while being treated with antibiotics and physiotherapy. A nasal biopsy using a microcurette was performed. During hospitalization the mother was taught how to aspirate mucus and to do postural drainage.

The child, now 37 months old, was followed in the outpatient clinic. He was not placed in a nursery, and contact with sick persons was avoided. During the 37 months of observation, the child had no pulmonary or ear, nose, and throat infections. Physiotherapy was performed two times daily, with obvious benefit. At 36 months a control biopsy was performed. Samples of nasal epithelium were also obtained from two newborns with hyaline membrane disease, two with meconium aspiration, and two with bacteriologically proven pulmonary infection. Following parental consent a biopsy was performed in a normal newborn baby who was born to a healthy woman following an uneventful pregnancy.

Methods and Results

Nasal biopsies were obtained from the newborns by brushing the lower surface of the nasal turbinate. The technique was simple and minimally invasive. Biopsies were fixed in glutaraldehyde and postfixed in osmium tetroxide in a cacodylate buffer. Thin sections were cut and studied by electron microscopy (Department of Anatomopathology, Professor W. Gepts). The first nasal biopsy in the...
patient with situs inversus revealed the absence of dynein arms from
the outer doublets (Fig 1) and abnormal orientation of the cilia (Fig
2). Compound cilia (Fig 3) were present, and other variations on
the normal nine plus two microtubular arrangement were found (pre-
ence of an extra central pair and missing peripheral microtubules).
These findings are consistent with the immotile cilia syndrome. The
second biopsy was also studied by phase-contrast microscopy; only a
few ciliated cells were motile, and the ciliary beats were uncoordi-
nated. Electron-microscopic findings were identical to those found
in the first biopsy.

Nasal biopsies of all of the other newborns were completely
normal. The orientation and structure were consistent with those
found in older children and adults; no compound cilia were present.

**DISCUSSION**

Immotile cilia have been reported earlier in the neonatal
period but without the ultrastructural study of the ciliary
defects at such an early age. In one case, electron-
microscopic examination of the nasal mucosa of a three-week-
old boy was inconclusive. A second biopsy at 21 months
confirmed the clinical diagnosis and showed a lack of ciliary
orientation and absent dynein arms. The immotile cilia
syndrome was suspected in our patient because of the situs
inversus. Rossman et al showed that dynein-defective cilia
were capable of motion; abnormal phase-contrast micro-
scopic findings and ultrastructural abnormalities were associ-
ated in our patient. To investigate whether the ultrastructural
abnormalities could possibly be linked with the age and not
with the disease, a biopsy was performed on a healthy
newborn in the same age group; normal structural findings
were obtained. Abnormal ultrastructural findings and func-
tion were present only in the newborn with situs inversus and
not in newborns with various neonatal pulmonary diseases.

The neonatal diagnosis is an important argument for the
primary defect of the disease. Some abnormalities regarded
as nonspecific lesions are found in patients with asthma or
sinusitis and in smokers. Five percent of the cilia of healthy
subjects had ultrastructural abnormalities; however, the
complete ciliary configuration of our healthy newborn was
normal. Lee and Rossman described an infant with hyaline
membrane disease that evolved into bronchopulmonary
dysplasia and was associated to ciliary defects; the lesions
were reversible, and normal ciliary motion was observed.
The nasal specimens of our two patients were obtained early
in the course of the disease and were normal.

Different authors described the importance of perform-
ing clearance studies to correlate with the ultrastructural
findings. The use of radioactively tagged test aerosol or
saccharin to measure the mucociliary transport is extremely
difficult to perform in neonates and children; a certain
 collaboration of the patient is mandatory for this method, and
these tests could not be performed in our study.

It was suggested by Carson et al that anomalies of the
ciliary microtubular system may not only be congenital but
also acquired. Our observations confirm that a good corre-
lation between clinical symptoms and microscopic changes
can be found in children; changes of the ciliary ultrastructure
in our patient can only be congenital. Recognition of the
immotile cilia syndrome in childhood is potentially signif-
cant, since treatment may delay or prevent the onset of
bronchiectasis. With prophylactic advice and daily treat-
ment, our patient did not have any infection during the first
37 months of observation. To the best of our knowledge, this
is the first report of the entity, including all of the structural
abnormalities, at such an early age. In contrast with older
children, ciliary defects in the newborn were never of the
acquired type in our group. In cases where no situs inversus
is present, the diagnosis at an early age is difficult. Examina-
tion of ciliary ultrastructure in the early neonatal period is
indicated in newborns with respiratory distress syndrome
when an immotile cilia syndrome is suspected.

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A 57-year-old woman with squamous carcinoma of the right lung (hilum) developed acute massive hemoptysis with syncope and hypotension. Resuscitation was complicated by the development of massive systemic air embolus, and the patient died.

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CASE REPORT

A 57-year-old black woman was diagnosed by bronchoscopy as having squamous cell carcinoma of the lung involving the right hilum. She was not considered a surgical candidate because of probable mediastinal involvement and was therefore treated with irradiation using opposed anteroposterior ports. The patient received a split course to the right hilum and mediastinum consisting of 2,000 rads at the time of diagnosis, followed by an additional 2,000 rads one month later. Follow-up chest roentgenograms at two and three months after diagnosis revealed no reduction in the size of the tumor. Atelectasis of the right lower lobe and a right-sided pleural effusion developed. Four months after diagnosis, while at home, the patient developed massive hemoptysis, quickly followed by syncope. Paramedics, finding the patient in a pool of blood, began resuscitative measures.

In the emergency room the patient was pulseless and apneic, with a junctional bradycardia. Endotracheal intubation was accomplished quickly, revealing extensive clots in the posterior pharyngeal airway and trachea. Ventilation was noted to be difficult because of high


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