Review article

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MECONIUM ILEUS

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Meconium ileus is congenital mechanical obstruction of the small intestine appearing as a result of the amended meconium. It is responsible for a third of small bowel obstruction in infants and is manifested in about 30-40% of children with cystic fibrosis. Patients with mutations in the CFTR gene and cystic fibrosis have abnormal chloride conductance through external cell membranes resulting in precipitation of thick secret in the respiratory tract, pancreas, liver, intestines and sweat glands. Maternal history and ultrasound during pregnancy allow the prediction which children will have the risk of meconium ileus. Meconium ileus occurs in 2 formats: a simple (67%) and complex (33%). The most common complications are: volvulus, atresia, meconium peritonitis, pseudocystic formation or perforation of the colon. The conservative treatment is based on the application of hyper or iso-osmolar contrast. A contrast enema is performed during fluoroscopy, gradually increasing intraluminal pressure in order to avoid possible perforation. In case of failure of conservative treatment, further treatment must be surgical. There are several surgical options of treatment (most commonly: Mikulicz, Bishop-Koop and Santulli) applied in order to provide the lowest possible bowel resection and enterostomy formation for possible postoperative irrigation. Long-term survival of patients with meconium ileus and cystic fibrosis is 83-90%.

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Introduction

Meconium ileus is congenital mechanical obstruction of the small intestine appearingas a result of the amended meconium (1). It was first described in 1905 (2), and in 1938, Anderson described and explained the connection between cystic fibrosis and meconium ileus (3). It is responsible for a third of small bowel obstruction in infants, manifested in about 30-40% of children with cystic fibrosis (4). Meconium ileus is the earliest clinical sign of cystic fibrosis, and because of this patients are diagnosed and treated in the neonatal age (5). Cystic fibrosis is an autosomal recessive disorder that appears in the white race in 1 of 29 live births, while it is rare in the black race (1/17 000) (3). Genetic substrate comprises a mutation in the CFTR (cystic fibrosis transmembrane conductance regulator) gene encoding the activity of chloride ion guide. Patients with CFTR gene mutations and cystic fibrosis have abnormal chloride conductance through external cell membranes, resulting in precipitation of thick secretions in the respiratory tract, pancreas, liver, intestines and sweat glands (6). Meconium ileus may be associated with intestinal atresia and congenital defects of the anterior abdominal wall (7).

Incidence

Meconium ileus is the cause in 9-33% of all neonatal intestinal obstruction, with an incidence of 1:2500 newborns. It is the third most frequent cause of neonatal intestinal obstruction, after ileo and duodeno-jejunal atresia and malrotation (2). It occurs in about 30-40% of children with cystic fibrosis (4).

Pathogenesis

Meconium ileus is always associated with cystic fibrosis, an autosomal recessive disease which is typical dysfunctional transfer of chloride ions across epithelial cells. This is due to quantitative or qualitative CFTR protein related disorders affecting multiple organ systems: intestines, pancreas, sweat glands, liver and salivary glands. The pancreas is the most

commonly affected organ because of the retention of juices and progressive atrophy of the acinar cells occurring in fetal life, in contrast to pulmonary mucosal plaque in the lower respiratory tract with a respiratory insufficiency during puberty. In 1989, the gene CFTR is detected. It is normally located on the apical membrane of epithelial cells of the stomach to the colon. The mutation of the CFTR gene on chromosome 7 is responsible for the development of cystic fibrosis. The most common mutation is ΔF508 and can be identified by DNA test used in neonates as well as family members who are considered to be potential carriers of the gene (2).

Clinical signs

One of the signs is polyhydroamnion during pregnancy, found in high intestinal obstruction and in 20% of mothers. The existence of fetal bowel hyperechogenicity on ultrasound, associated with bowel dilatation or ascites may indicate intestinal obstruction. Meconium begins to fulfill the small intestine during the 20th week of gestation, so the identification of meconium ileus before that period is rare (7). History of mother's ultrasound during pregnancy allows the prediction that the children will have the risk of meconium ileus (3). Meconium ileus occurs in two forms: a simple (67%) and complex (33%). The most common complications are: volvulus, atresia, meconium peritonitis, pseudocystic formation or perforation (1). If abdominal distension, intermittent vomiting with mixture of bile, and without meconium stools occur in the first 8 hours of life, it is a simple form of meconium ileus. By clinical examination it is possible to palpate dilated intestinal loops in the right lower abdominal quadrant; furthermore digital rectal examination found an empty rectum. Unlike simple forms, complex forms of meconium ileus occur in the first 24 hours of life of the newborn. The abdomen is distended with pronounced veins of the abdominal wall. Bowel necrosis and perforation resulting in peritonitis may arise as complications. Sometimes after meconium perforation, a pseudocyst can occur as a palpable mass in the right lower abdomen, and the skin over the mass is edematous and transparent (1,2).

Diagnosis

Neonates with meconium ileus are often born with distension of the abdominal wall, which is the only difference between children with bowel obstruction in which distension occurs after air swallowing. Peristaltic waves are visible, and can often be palpable as solid gyrus intestine. In many children, digital rectal examination found an empty rectum. Diagnosis of meconium ileus based on clinical examination includes radiological examination of the abdomen. Intestinal distension a dominant sign. Characteristic radiographic signs are distended intestinal convolutions, without or with little air in the intestines above meconium content. The most common sign is in the right hemiabdomen, present like air between meconium content that resembles the appearance of a soap bubbles. Radiographic signs of complicated meconium ileus may be different. Diffuse calcification in the abdomen present on the plane radiograph of the newborn indicates intrauterine intestinal perforation and meconial peritonitis (3). Meconium ileus is associated with cystic fibrosis, and the most important test in the diagnosis of cystic fibrosis is a sweat test which measures the concentration of sodium chloride. The concentration of these chloride ions must be greater than 60 mEq / L in 100 mg of sweat. In newborns, it is often difficult to collect sufficient amount of sweat in order to do the necessary analysis, so sometimes it is necessary to repeat the test several times. Children with cystic fibrosis as well as heterozygous carriers of the gene can be revealed with this method. Increased serum immunoreactive trypsin (IRT) may indicate cystic fibrosis, but must be confirmed by other tests (2).

Differential diagnosis

Differential diagnosis of all causes of distal intestinal obstruction should be considered. They include: Hirschsprung's disease, small bowel atresia, meconium plug syndrome and small left colon neonate (8). Meconium ileus, distal intestinal obstruction and constipation can often be different varieties that accompany cystic fibrosis (9).

Treatment

Meconium ileus can be treated conservatively and surgically. The first step in treatment of meconium ileus requires installation of nasogastric tube, antibiotic prophylaxis and correction of dehydration, electrolyte and hypothermia. The conservative treatment includes applying of hyper or iso-osmolar contrast. Recent studies show the effectiveness of the gastrografin of 20-50%. The goal of contrasting enemas is to soften and moisturises meconium for easier bowel emptying. Contrast enema is applied under the control of fluoroscopy, gradually increasing intraluminal pressure in order to avoid possible perforation. Fifty percent of children treated with contrast enema do not require further treatment, while some may need to repeat enema. Radiological images are repeated after 3, 6, 12, 24 and 48 hours to monitor the occurrence of possible complications (2.10). Conservative treatment is applied if there is no intestinal atresia, volvulus, gangrene bowel perforation and meconium peritonitis. If conservative treatment is not successful, surgical treatment is optimal option for cases of complicated meconium ileus. The goal of surgery is the evacuation of meconium from the intestines and the preservation of greater length of the intestines (10). There are several surgical techniques (Mikulicz, Bishop-Koop and Santulli enterostomy) for postoperative intestinal irrigation that can be performed even in extremely small birth-waight premature infants (11). In the next step, closure of the stoma and intestinal anastomosis should be planned (1). In some cases, it is possible to perform segmental intestinal resection with primary anastomosis creation (12).

Prognosis

Meconium ileus is the first sign that points to the existence of cystic fibrosis. In complicated forms of meconium ileus, obstruction of the small intestine may occur, while in uncomplicated forms of conservative treatment complications are rarely seen. In recent years, survival of newborns with meconial meconium ileus has improved and reached about 90% thanks to intensive care, improved surgical techniques and medical treatment. Long-term survival of patients with meconium ileus and cystic fibrosis is 83-90% (2).

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MEKONIJALNI ILEUS

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Mekonijalni ileus je kongenitalna mehanička opstrukcija tankog creva koja je nastala kao posledica izmenjenog mekonijuma. Odgovoran je za trećinu opstrukcija tankog creva kod novorođenčadi, a manifestuje se u oko 30-40% dece sa cističnom fibrozom. Bolesnici sa CFTR mutacijama gena i cističnom fibrozom imaju nenormalnu provodljivost hlorida preko spoljnih ćelijskih membrana, što rezultira precipitacijom gustog sekreta u respiratornom traktu, pankreasu, jetri, crevima i znojnim žlezdama. Anamneza majke i ultrazvučne pretrage tokom trudnoće omogućavaju predikciju koja će deca imati rizik od nastanka mekonijalnog ileusa. Mekonijalni ileus se javlja u dva oblika: jednostavni (67%) i komplikovani (33%). Od najčešćih komplikacija navode se: volvulus, atrezija, mekonijalni peritonitis, pseudocistična formacija ili perforacija kolona. U konzervativnom lečenju primenjuje se hiper ili iso-osmolarni kontrast. Kontrastna klizma se primenjuje pod kontrolom fluoroskopije, postepenim povećanjem intraluminalnog pritiska kako bi se izbegla moguća perforacija. U slučaju neuspeha konzervativnog lečenja, dalje lečenje je hirurško. Postoji nekoliko hirurških opcija lečenja (najčešće korištene su: po Mikuliczu, Bishop-Koopu i Santulliju), a koje se svode na najmanju moguću resekciju creva i formiranje enterostomije kroz koju će biti moguća postoperativna irigacija. Dugoročno preživljavanje bolesnika s mekonijalnim ileusom i cističnom fibrozom iznosi 83-90%, ali je moguća pojava fibrozne kolonopatije i endokrine disfunkcije.

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Ključne reči: *ileus mekonijalis, neonates, lečenje*