Meconium Disease

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Outlines

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- Meconium plug syndrome
- Neonatal small left colon syndrome
Introduction

• The term **meconium disease** refers to **meconium ileus** and **meconium plug syndrome**

• considered separately from functional or anatomic causes of neonatal intestinal obstruction, such as Hirschsprung disease, intestinal atresia, and anorectal malformations
Meconium is the earliest stool of a mammalian infant.

Unlike later feces, meconium is composed of materials ingested during the time the infant spends in the uterus: intestinal epithelial cells, lanugo, mucus, amniotic fluid, bile, and water.
Meconium compositions

• Sodium, Potassium, Magnesium: twice lesser
• Enzyme-catalyzing heavy metals, protein nitrogen: higher
• Carbohydrates: lesser
• Most of proteins: albumin (believed to be plasma in origin)
  • Diagnostic screening tool for meconium ileus
Meconium Ileus (MI)

- One of the most common causes of intestinal obstruction in the newborn (9-33%)
- Extremely viscid, protein-rich, inspissated meconium causing an intraluminal obstruction in the distal ileum, usually at the ileocecal valve
- **Earliest** clinical manifestation of cystic fibrosis (16-20.8%)
- Although MI can occur with other uncommon conditions such as pancreatic aplasia and total colonic aganglionosis, it is often considered **pathognomonic for CF**
Meconium Ileus (MI)

- **MI** is presented with more severe form of CF (20% & related with diminished pulmonary function)

- **A family history of CF**: presents in 10-33% of patients with meconium ileus

- **Due to abnormalities of exocrine mucus secretion and pancreatic enzyme deficiency** → less water content (65% vs 75%) when compared to normal meconium, lower sucrase and lactase levels, increased albumin, and decreased pancreatic enzymes
Cystic fibrosis

• Most common, potentially lethal genetic defect affecting Caucasians
• An inherited autosomal recessive disease with a 4–5% carrier rate
• The incidence of CF is much lower in non-Caucasian populations
  • 1:10,500 Native American Aleut births, 1:13,500 in Hispanic–Caucasian births, 1:15,000 African–American births, 1:31,000 in Asian–American births
• Clinicals: chronic obstruction and infection of the respiratory tract, insufficiency of the exocrine pancreas, and elevated sweat chloride levels
Cystic fibrosis: Genetics

• CFTR (Cystic fibrosis transmembrane regulator) mutations
  • F508del: M/C mutations in CFTR (removal of a phenylalanine residue at amino acid position 508)
    • 70% of abnormal CF genes
CFTR (Cystic fibrosis transmembrane regulator) mutations
Cystic fibrosis: Genetics

- Congenital bilateral **absence of the vas deferens** (CBAVD): F508 del and G551D mutations
- G551D is the third most common CF-associated mutation
  - pancreatic insufficiency, pulmonary symptoms, and an episode of MI equivalent, indicating **CBAVD may be associated with a more severe CF phenotype**
Cystic fibrosis: GI Pathophysiology

• Characterized by mucoviscidosis of exocrine secretions throughout the body resulting from abnormal transport of chloride ions across apical membranes of epithelial cells

• Pancreatic insufficiency plays a central role in the pathogenesis of MI

• Congenital stenosis of the pancreatic ducts is associated with meconium-induced bowel obstruction
Cystic fibrosis: GI Pathophysiology

- 10% of patients with CF are pancreatic sufficient and tend to have a milder course
- A prevalence of intestinal glandular abnormalities contribute more significantly to the production of abnormal meconium
- Abnormal intestinal motility may also contribute to the development of MI
Cystic fibrosis: Prenatal Diagnosis and Screening

- ACOG recommends all women of reproductive age should be offered CF carrier screening.
- The antenatal diagnosis of MI can be made in two different groups: a high-risk group and a low-risk group.
  - Low-risk group: sonographic appearances of MI are found on routine prenatal ultrasound in a mother with a negative CF carrier screen.
  - High-risk group: sonographic findings consistent with MI in a fetus with carrier parents, pregnancies subsequent to the birth of a CF-affected child.
Cystic fibrosis: Prenatal Diagnosis and Screening
Algorithm for antenatal management

Prenatal US @ GA 15-21 wk suspicious for MI

Prenatal CF carrier screening by buccal brushing

One or no CF mutations identified

Two CF mutations identified
Algorithm for antenatal management

1. Prenatal CF carrier screening by buccal brushing
2. One or no CF mutations identified
3. Previous child with CF
   - No
   - Yes
Algorithm for antenatal management

1. Previous child with CF
   - No
     - F/U US q 6 wk
     - Resolution of US findings
     - Continued suspicion of MI
   - Yes
     - RFLP testing of parent and affected child
     - Amniocentesis
     - Referral to tertiary care center
Algorithm for antenatal management

Prenatal CF carrier screening by buccal brushing

Two CF mutations identified

Amniocentesis

Amniocentesis refused

Referral to tertiary care center

2 mutations or (+) RFLP in fetus

<2 mutations or (-) RFLP in fetus

F/U US q 6 wk

Resolution of US findings

Consider termination
Meconium Ileus: sonographic evaluation

• A hyperechoic, intra-abdominal mass (inspissated meconium), dilated bowel, and non-visualization of the gallbladder
  • Normal fetal meconium, when visualized in the second and third trimesters, is usually hypoechoic or isoechoic to adjacent abdominal structures

• In addition to MI, **hyperechoic bowel** has been reported with Down syndrome, intrauterine growth retardation, prematurity, in utero cytomegalovirus infection, intestinal atresia, abruptio placenta, and fetal demise
Meconium Ileus: sonographic evaluation

• Hyperechoic fetal bowel: related to gestational age at detection, ascites, calcification, volume of amniotic fluid, and the presence of other fetal anomalies
  • Hyperechoic bowel has been found to be a normal variant in both the second and third trimesters
Meconium Ileus

• DDx for **bowel dilatations**: midgut volvulus, congenital bands, intestinal atresia, intestinal duplication, internal hernia, meconium plug syndrome, and Hirschsprung disease

• DDx for **absent gallbladder**: meconium ileus, biliary atresia, omphalocele, diaphragmatic hernia, chromosomal abnormalities, and a normal pregnancy
Clinical Presentation

- Categorized as either **simple** or **complicated**
- **Simple MI**: without atresia/ volvulus/ perforation/ ischemia
  - appear healthy immediately after birth
  - within 1 to 2 days, they develop abdominal distension and bilious emesis
  - Normal meconium will not be passed
  - rectum and anus are often narrow (misinterpreted as anal stenosis)
Clinical Presentation

- **Complicated MI**: with atresia/ volvulus/ perforation/ ischemia/ signs of sepsis or shock
  - symptoms within 24 hours of birth
  - 12–17% of neonates born with jejunoileal atresia have CF
  - **ALL** neonates with jejunoileal atresia and an abnormal meconium presentation (MI, meconium plug syndrome, giant cystic meconium peritonitis, etc.) should undergo a sweat chloride test
  - Incidence of CF in neonates with meconium peritonitis: 15–40%
Clinical Presentation

• 4 types of meconium peritonitis:
  • adhesive meconium peritonitis
  • giant cystic meconium peritonitis or pseudocyst
  • meconium ascites
  • infected meconium peritonitis

• The site of perforation is usually closed by birth, if not closed → increased mortality
Radiographic features

- Distal SBO
- Soap bubbles
- Microcolon
Radiographic features

Simple MI

Ground-glass appearance at RLQ
Radiographic features

**Complicated MI**

*Speckled calcification:* intrauterine intestinal perforation and meconium peritonitis

*1/3 no radiographic finding shows complication*
Radiographic features

‘microcolon of disuse,’ often containing small, inspissated rabbit pellets (scybalae) of meconium

* If contrast cannot be refluxed into the dilated small bowel, operative exploration is required for diagnosis and therapy.
Screening tools

• A tetrabromophenolethylester blue indicator: meconium albumin concentrations in excess of 20 mg/g of stool
  • false-positive: prematurity, melena, gastroschisis, and intrauterine infection
• Stool trypsin and chymotrypsin analysis: less than 80 mg/g of stool
Diagnostic Testing

• established with a **sweat test**
  • $[\text{Na}] = 60 \text{ mmol/L in 100 mg} \rightarrow \text{diagnostic}$
  • $[\text{Na}] = 40-60 \text{ mmol/L in 100 mg} \rightarrow \text{intermediate}$
  • $[\text{Na}] = <40 \text{ mmol/L in 100 mg} \rightarrow \text{normal}$

• Neonatal CF screening programs using the **Guthrie blood spot test** for raised concentrations of immunoreactive trypsinogen with **CFTR mutation analysis**
Nonoperative Management of Simple Meconium Ileus

• **Initial Mx** like intestinal obstruction: volume resuscitation, gastric decompression, empiric antibiotics

• **Specific Mx**: isotonic water-soluble contrast enema under fluoroscopic control (but need adequate IV resuscitation)
  - Inflation of the catheter **balloon should be avoided** to minimize the risk of perforation****
  - **Warm saline** enemas containing 1% **N-acetylcysteine** may help evacuate meconium
  - **Radiographs** should be obtained as clinically indicated to confirm evacuation of the obstruction and to exclude late perforation
Nonoperative Management of Simple Meconium Ileus

• If evacuation is incomplete, or if the first attempt at contrast enema evacuation does not reflux contrast into dilated bowel, a second enema may be necessary

• After two failed attempts at nonoperative water-soluble enemas, operative intervention is likely warranted

• However, if progressive distension, signs of peritonitis, or clinical deterioration occur, operative exploration is indicated
Nonoperative Management of Simple Meconium Ileus

• Following successful evacuation and resuscitation, 5 mL of a 10% N-acetylcysteine solution may be administered every six hours through a nasogastric tube to liquefy the upper gastrointestinal secretions

• Feedings with supplemental pancreatic enzymes for those infants confirmed with CF may be initiated when signs of obstruction have subsided
Nonoperative Management of Simple Meconium Ileus

- Potential complications with the use of enemas: rectal perforation, hypovolemic shock, bowel ischemia
Operative Management

- Simple MI: inadequate meconium evacuation or a complication from the contrast enema
  - At laparotomy, manual evacuation of the inspissated meconium can be aided by intraoperative instillation of 2% or 4% N-acetylcysteine or saline solutions
  - If necessary, a T-tube may be left through the enterotomy for the purpose of postoperative bowel irrigation, decompression, pancreatic enzyme instillation, and/or feeding
Operative Management

- **Complicated MI**: Operative management is almost always required in cases of complicated MI
  - **Except** in utero spontaneously sealed perforation with intact intestinal continuity and extraluminal intraperitoneal calcified meconium

- **Indications for operation**: peritonitis, persistent intestinal obstruction, enlarging abdominal mass, and ongoing sepsis

- **Surgical management**: debridement of necrotic material, pseudocyst resection, diverting stoma(s), antibiotics, and meticulous postoperative care
Operative Management

• The goal of operative management is the relief of intestinal obstruction and the preservation of maximal intestinal length
Postoperative Management

• Requires ongoing resuscitation, including maintenance fluids and replacement of insensible and gastrointestinal fluid losses

• Instillation of 2% or 4% N-acetylcysteine via a nasogastric tube, enterostomy tube, or via an ileostomy or mucous fistula

• Stomas should be closed when possible (four to six weeks) to avoid prolonged problems with fluid, electrolyte, nutritional losses, and cholestatic jaundice

• Nutritional management

• Pulmonary management
Nutritional management

• **Enteral feeds**: breastfeeding/infant formula with supplemental pancreatic enzymes and vitamins
  - Those with significant loss of intestinal length, initiating the enteral feeding with a predigested, diluted formula at low continuous volumes is best

• **Parenteral nutrition**: in complicated cases and enteral feeding is impossible
**Nutritional management**

- **Pancreatic enzymes**: 2,000–4,000 lipase units per 120 mL of full strength formula
  - Complications of pancreatic enzymes:
    - Fibrosing colonopathy from *excessive* enzyme doses
    - MI equivalent, or distal intestinal obstruction syndrome (DIOS) from *inadequate* enzyme therapy
Nutritional management

• **Gastric acid hypersecretion** is seen in patients who have short bowel syndrome: inactivates the pancreatic enzyme
  • H2 receptor given adjunct to pancreatic enzyme
• **Urine sodium** should be measured when there is growth failure (urine sodium <10 mEq/L: need sodium supplementation
Pulmonary management

- Prophylactic pulmonary care with chest physiotherapy should be initiated early in the postoperative period
- Head-down position should not be used as this increases the risk of gastroesophageal reflux (GER) and aspiration
- Infants should receive nebulized albuterol twice daily followed by chest physiotherapy
Prognosis

• Uniformly poor prior to mid 1900 (mortality rate up to 67%)

• Survival rates of 85 to 100% have been reported in uncomplicated MI, and up to 93% in complicated cases
  • Improved outcomes due to advances in prenatal diagnosis, pulmonary and neonatal intensive care, nutrition, antibiotics, anesthesia, operative management, and an improved understanding of the pathophysiology and treatment of the CF complications
• children with MI have worse lung function and more obstructive lung disease than those with CF but without MI
COMPLICATIONS OF MECONIUM ILEUS AND CYSTIC FIBROSIS

• Gastroesophageal Reflux Disease
• Biliary Tract Disease
• Distal Intestinal Obstruction Syndrome
• Appendicitis
• Intussusception
• Fibrosing Colonopathy
Gastroesophageal Reflux Disease

- Increased prevalence in patients with CF (80% in pt. < 5 yr)
- Pathological reflux with endoscopic and histological esophagitis: > 50% of CF
- Anti-reflux medications, modification of chest physiotherapy, and eliminating the 30° head-down tilt may all decrease the incidence of GER
- If unresponsive to medical management → anti-reflux procedure
Biliary Tract Disease

- Most common hepatic complications of CF are steatosis, fibrosis, biliary cirrhosis, atretic gallbladder, cholelithiasis, sclerosing cholangitis, and biliary dyskinesia.
- Obstruction of intrahepatic biliary ductules by abnormal mucoid secretions or inspissated bile, resulting from the absence of functional CFTR in bile duct epithelial cells, results in the development of cirrhosis in patients with CF.
- 13% of CF patients, only 4.2% manifest overt liver disease.
Biliary Tract Disease

- Liver transplantation has been successfully carried out in CF patients with ESLD who did not have respiratory failure.
- Gallbladder disease is prevalent in the CF population, including cholelithiasis in up to 24%, and abnormal cholecystograms in 46%.
  - Other abnormalities include microgallbladder, atretic cystic duct, and hyperviscous mucus.
- Symptomatic gallbladder disease in CF reported to be approximately 4% (stones: protein and calcium bilirubinate).
Distal Intestinal Obstruction Syndrome

• Formerly called MI equivalent
• a recurrent, partial or complete intestinal obstruction unique to teenage and young adult patients with CF that occurs secondary to abnormally viscid muco-feculent material in the distal ileum and right colon
• occurs in 15–37% of patients with CF
• Precipitating factors: sudden withdrawal of (or noncompliance with) enzyme supplementation, immobilization, dehydration, respiratory tract infections, and recovery from surgery
Distal Intestinal Obstruction Syndrome

- **Symptoms**: crampy abdominal pain, often localized to the right lower quadrant, and decreased frequency of defecation
- A supine and erect abdominal film is the most useful initial investigation: like film in infant with MI
- **Treatment**: colonic enema washout, a balanced polyethylene glycol-electrolyte solution (20-40 ml/kg/hr; Max 1200 ml/hr)
- Some authors have recommended DIOS prophylaxis with use of scheduled laxatives and high dietary fiber
Appendicitis

• As they are often already being treated with antibiotics and steroids, the classical clinical signs and symptoms of appendicitis are often masked → increased incidence of perforation

• If appendiceal perforation → initial treatment should be percutaneous drainage of the abscess and interval appendectomy

• If nonperforated appendicitis → appendectomy

• Many surgeons perform incidental appendectomy during other abdominal operations in CF patients
Intussusception

• Approximately 1% of children with CF with the average age of onset of 9.5 years
• The most common site for intussusception is ileocolic, but it may be ileoileal, cecocolic, or colocolic
• Abnormally thick stool adheres to the bowel wall, appendix: act as a lead point
• If unable to be reduced operatively, a bowel resection with anastomosis is required
  • The appendix should be removed at operation in patients with an intussusception
Fibrosing Colonopathy

• A result of **colonic strictures**, and presents with signs and symptoms of DIOS

• Patho: post-ischemic ulcer repair, erythematous cobblestone appearance to the mucosa, mucosal and submucosal fibrosis, and destruction of the muscularis mucosa

• Exposed to high doses of pancreatic enzymes and present with symptoms of abdominal pain, distension, chylous ascites, change in bowel habit, or failure to thrive
Fibrosing Colonopathy

- Barium enema: mucosal irregularity, loss of haustral markings with a foreshortened colon, and varying degrees of stricture formation
- Colonoscopy: erythematous mucosa with areas of narrowing (multiple biopsies should be done)
- Initial management: reduction of the enzyme dosage to 500–2500 lipase units/kg per meal
- Patients who show signs of unrelenting failure to thrive, obstruction, uncontrollable diarrhea, or chylous ascites will need operative intervention
Fibrosing Colonopathy

• The aim of operative intervention is to resect the affected bowel and perform a primary anastomosis but impossible with total colonic or rectal involvement
• Regular follow-up due to possible recurrence
Meconium plug syndrome

- Under normal conditions, the terminal two centimeters of neonatal meconium is firm in texture, forming a whitish cap.
- Most newborns pass this meconium cap before, during, or shortly after delivery.
- One in 500 newborns will have a longer, more tenacious obstructive plug.
- Presentation: same as meconium ileus.
- Fortunately, colon function is generally preserved and returns to normal following passage of the plug.
Meconium plug syndrome

• Pathologic causes of MPS include CF, small left colon syndrome, and Hirschsprung disease
  • Less common causes include congenital hypothyroidism, maternal narcotic addiction, and neuronal intestinal dysplasia

• A contrast enema may be therapeutic as well as diagnostic
Meconium plug syndrome

• Following resolution, a sweat test should be performed to exclude CF and a thyroid-stimulating hormone level should be obtained

• A rectal biopsy should be performed to evaluate for Hirschsprung disease if there is a dysfunctional stooling pattern after resolution of the plug
Neonatal small left colon syndrome

• Confined to the left colon, appears as a funnel-shaped tapering on contrast enema
• Often associated with a diagnosis of maternal diabetes, hyperthyroidism, drug abuse, or eclampsia
• Rectal biopsy is required to exclude Hirschsprung disease
• Other features of meconium ileus are usually not present
Conclusion

• Meconium disease: Meconium ileus, Meconium plug syndrome
• Differential diagnosis: Jejunoileal atresia, Hirschsprung’s disease, Total colonic aganglionosis, neonatal small left colon syndrome
• Multidisciplinary managements
• Prognosis: much better in 2000s
References

• Ashcraft’s pediatric surgery, 6th edition
• Coran’s pediatric surgery, 7th edition
Thank you
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