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Clinical Audit

Meconium Ileal Obstruction and Functional Immaturity of the Intestine (MIOFI) in Extremely Premature neonates: A Case Series

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Keywords
Acute abdomen
Intestinal obstruction
Meconium disorders
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Abbreviations
ELBW - Extremely low birth weight
MI - Meconium ileus
MIOFI - Meconium ileal obstruction with functional immaturity of the intestine
NEC - Necrotizing enterocolitis
NICU - Neonatal intensive care unit
SGA - Small for gestational age
VLBW - Very low birth weight

Abstract

Introduction: *Thick meconium induced ileal obstruction due to functional immaturity of the intestine (MIOFI) is a rare and frequently unrecognized condition that is typically seen in extremely low birth-weight (ELBW) and low birth-weight (LBW) premature babies. Its prognosis depends on early recognition and treatment. This retrospective study was performed to analyze the spectrum of babies with MIOFI and their outcome.*

Methods: *A retrospective review of neonates presenting to two referral hospitals with MIOFI during the first semester of 2024 was performed.*

Results: *During the study period 3 neonates presented with MIOFI. All of them were product of complicated pregnancies. Two of them were of ELBW. All the babies passed minimal amount of meconium prior to the onset of MIOFI symptoms. Two of them had severe abdominal distension without air-fluid levels and 1 presented with gasless abdomen. Only one was operated upon, with a mistaken clinical diagnosis of long-segment aganglionic megacolon; the other two were treated conservatively. All the 3 babies showed normal intestinal function during follow-up.*

Conclusions: *MIOFI presents as neonatal intestinal obstruction affecting the distal ileum. Diffuse abdominal distention and respiratory distress are common symptoms. MIOFI responds well to water-soluble contrast enemas, with elimination of meconium plugs and mucus, followed by normalization of intestinal transit.*

INTRODUCTION

Thick meconium induced ileal obstruction due to functional immaturity of intestine (MIOFI) was first described in 1965.[1] The disease is rare with an incidence of 1-2 patients per 1,000,000 live-births[2] and it is typically seen in extremely low-

(ELBW) and very low- birth-weight (VLBW) premature babies. The condition has also been rarely described in term neonates.[3-4] Although MIOFI is not well known and is rarely considered in the differential diagnosis, its prevalence is increasing due to improved survival of extremely premature babies in recent years.[5] The reported prevalence of MIOFI in ELBW premature babies varies from 3.9 to 17%.[6,7]

Lack of familiarity with the entity among clinicians is the first barrier of early diagnosis and prompt management.[8] A correct diagnosis is essential for improved outcome and avoidance of unnecessary surgical intervention and its associated morbidity. In this communication we report a small cohort of MIOFI to create clinical awareness.

METHODS

Retrospective review of all neonates presenting with MIOFI during the first half of 2024 at two referral hospitals for high-risk pregnancy and surgical care of neonates in Rio de Janeiro, Brazil was performed. Parental consent to use clinical data was obtained.

RESULTS

A total of 3 neonates presented with MIOFI during the study period. Their clinical details are summarized in Table 1. Two of them were ELBW premature babies. Prior to the onset of MIOFI symptoms, all of them had delayed elimination of meconium, either after anal stimulation (n=2) or spontaneously (n=1). Abdominal distension was severe in all the neonates, and it caused respiratory distress in 2 of them. (Fig. 1) Plain radiographs of two neonates showed diffuse gaseous distension of abdomen without air-fluid levels (Fig. 2), while one presented with gasless abdomen (case 2).

Only one patient (case 3) was operated on day-26 with a mistaken clinical diagnosis of long-segment aganglionic megacolon. Intraoperatively the surgeon noted micro-colon and a transition zone 5 cm proximal to ileocecal junction. Viscid meconium in the distal ileus was difficult to be milked distally. Ileostomy 10 cm proximal to the ileocecal valve and colonic biopsy were done. Persistent abdominal distension necessitated a re-operation after 6 days. He passed meconium after retrograde contrast enema through the ostomy.

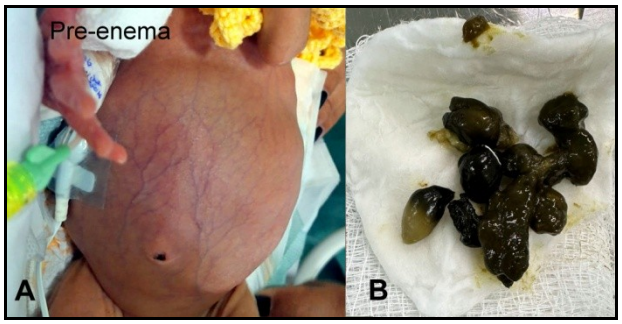

Fig 1. *Clinical features of MIOFI. (A) Severe abdominal distension (B) Thick meconium eliminated after enema (Patient 2)*

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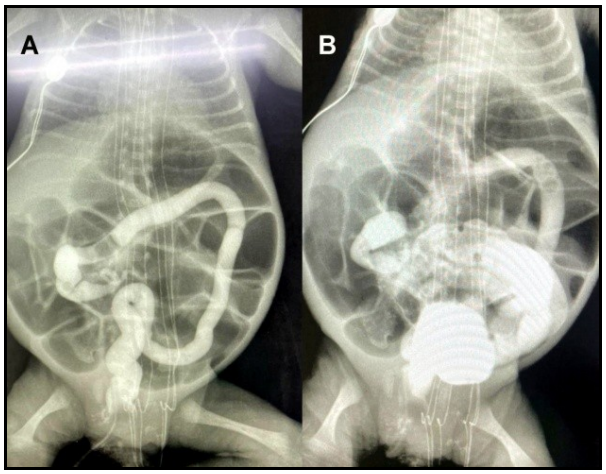

Fig 2. *Radiographs in MIOFI showing severe intestinal distention without air-fluid levels. (A) Gastrografin™ enema showing microcolon, (B) Contrast refluxes into the ileum proximal to the obstruction (Patient 1)*

The other two patients were treated conservatively as non-perforated MIOFI. Patient 1 was relieved after achieving ileal reflux of contrast through a retrograde enema (Fig. 2) and patient 2 resolved after administering high-volume saline enema.

Table 1. Clinical features of neonates with MIOFI

Clinical features	Case 1 §	Case 2	Case 3
Sex of newborn	Male	Male	Male
Birth weight (g)	770	895	1765
Gestational age at birth (weeks)	29	26	33
Mode of Delivery	Cesarean (emergency)	Vaginal	Cesarean (emergency)
Maternal co-morbidity	hypertension, syphilis	Premature amniorrhexis with infection, syphilis.	Hypertension
Onset of obstructive symptoms	Day 10 of life	From birth	Day 5 of life
Symptoms	AD, FI, RD, no sepsis	Severe AD	FI, no sepsis, worsened AD on day 26, RD
Age at first elimination of meconium	Day 5 of life by anal stimulation	Day 5 of life by enema	72 hr of life, Spontaneous
Plain Radiographs	Diffuse gaseous distension	Gasless abdomen	Diffuse gaseous distension
Treatment	Gastrografin™ enema twice	Saline enema	Harmann-type terminal ileostomy + colon biopsies
Colonic biopsy	Not done	Not done	Ganglion cells present
Outcome	Passed meconium.	Passed meconium on day 23	Non-functional ileostomy needed contrast enema.
Complications	Intestinal hemorrhage* and shock*.	Barotrauma†, Pneumoperitoneum†(on day 7 treated with flank drain), Operative liver laceration, Endocarditis*, Superior vena cava thrombosis*	None
Follow up	Died on day 29 of life.	Died on day 45 of life	Awaiting ileostomy closure.

** Complications following MIOFI; † Complications before the onset of MIOFI. § - Cystic fibrosis excluded by genetic test. AD - Abdominal distension, FI - Feed intolerance, MIOFI - Meconium ileal obstruction with functional immaturity of the intestine, RD - Respiratory distress*

All the three neonates had normal intestinal function after the elimination of huge volume of extremely thick meconium. Only one patient survived and is waiting to have his ileostomy closed. Two other neonates died 6 and 22 days respectively after the resolution of MIOFI; they died of unrelated causes such as intestinal hemorrhage, catheter sepsis, endocarditis associated to superior vena cava thrombosis.

DISCUSSION

The literature about MIOFI is scarce and the entity is not well known to pediatricians and pediatric surgeons.[9] In the literature, MIOFI is known by several synonyms. (Table 2) This variable nomenclature hampers research and accentuates difficulties in differential diagnosis, possibly leading to late or misdiagnosis and delayed treatment.

Intestinal function matures in the last trimester of pregnancy. Immature neural ganglia that predominate the enteric nervous system till 24 weeks of gestation gradually matures.[10] Intestinal peristalsis is typically disorganized between 25-30 weeks of gestation, generating inefficient propulsion.[5] Hence, delayed elimination of meconium is not uncommon in ELBW preemies.[5-6]

Table 2. Synonyms of MIOFI

Names stressing its resemblance to meconium ileus*
• Meconium ileus equivalent
• Meconium ileus without cystic fibrosis
Names emphasizing its high incidence in preemies
• Meconium obstruction of prematurity
• Neonatal transitory ileus
Names emphasizing the abnormal nature of meconium
• Meconium disease
• Thick meconium syndrome
• Meconium-related ileus
Names emphasizing the immaturity of intestine
• Micro-colon of prematurity
• Neonatal functional intestinal obstruction

** Classical meconium ileus occurring in cystic fibrosis*
MIOFI - Meconium ileal obstruction with functional immaturity of the intestine.

MIOFI presents as acquired distal ileal obstruction with diffuse abdominal distention which may be complicated by respiratory distress.[11,12] Prenatal intestinal abnormalities are usually absent. Prior to the onset of MIOFI, most of the neonates pass small amount of meconium, either spontaneously or after enema.[5,13] Term neonates present earlier, while ELBW and preterm babies become symptomatic during the second week of life.[11,13] Typical cases do not present with sepsis or peritonitis. They show a relatively good clinical condition, except after perforation.

Air-fluid levels are absent in plain radiographs.[8] Absence of rectal air shadow may raise a suspicion of aganglionic megacolon.[11,14] Rarely, a gasless abdomen is seen as it was in our case-2.[15-16]. Pneumoperitoneum may occur with perforation. In premature neonates presenting with typical clinical features an empirical diagnosis of MIOFI should be assumed.

Colonographically or intraoperatively a change in the caliber of the distal ileum (10 - 30 cm proximal to the ileocecal valve), resembling the transition zone of a *total colonic aganglionosis*, may be seen. Multiple filling defects (meconium plugs) are seen distal to the obstruction. Long thick meconium moulds seen within the obstructed bowel are difficult to manipulate or milk down digitally. The colon may either be normal or be a microcolon.[9]

Histologically, neural ganglion cells are present in the entire bowel, as demonstrated in the case-3 of our series. Ganglion cells of MIOFI are typically immature, a fact that differentiates it from typical aganglionic megacolon.[2,10]

Most patients respond to water soluble contrast enema treatment with diatrizoate meglumine and diatrizoate sodium solution-USP (Gastrografin™, Bracco Diagnostics, Italy). It was adapted from the cystic fibrosis treatment described by Noblett[17] in 1969. Hyperosmolar contrast dissolves viscid meconium facilitating its passage whereupon the intestinal transit becomes normalized. Technical details of enema such as the frequency of administration, volume of enema fluid and ratio of dilution are variously proposed by different authors.[6,19-20] Gastrografin™ dilution of 1:5 to 1:4 is commonly used. The total irrigation fluid per enema ranges from 10-15 ml/kg to 20 ml/kg. Retrograde infusion of contrast solution may be done by passive irrigation under gravity, pressure controlled ($\leq$ 50 cmH_2O)[13] or flow controlled (1 ml/s).[6,22] Irrigation may be done with or without rectal occlusion with a balloon catheter[17-20] and it may be given once[6,16,19] or twice[18,22] daily. Administration of enema under real-time fluoroscopy monitoring is not essential.[18] Most of the clinicians avoid risky transportation of sick babies to a radiology suite and they prefer bedside 'blind' infusion in the neo-

natal intense care unit controlled with post-infusion imaging[6,13,19,22] or real-time ultrasound.[20] Timing of enema administration is also not well defined. But it seems logical, to administer enema treatment if a newborn with distended abdomen did not pass meconium within the first 48 hr of birth. Most of the authors[12-13,19,21,22] agree that contrast refluxing into the ileum is essential for satisfactory therapeutic response. Criteria of diagnosing inadequate response to enemas and surgical indications are mostly subjective, with the exception of perforation complicating the treatment. Enemas are generally safe, and only 3 perforations associated with them are described in the literature.[7-9] One of the perforations occurred 8 hours after the procedure.[9] Enema is relatively contraindicated in hemodynamically unstable neo nates, due to the risk of osmotic dehydration.

Most neonatal surgeons opt for intra-operative lavage (including transappendicular irrigation) or milking of inspissated meconium with or without decompressing ileostomy. Simple abdominal drain is not sufficient to treat perforations; rather the intrinsic obstruction should to be addressed.[8,13] With successful treatment, reasonably good survival with normal gut function has been reported.

The close differential diagnosis of MIOFI includes meconium ileus secondary to cystic fibrosis, meconium plug syndrome, long segment colonic aganglionosis and ileal atresia. Complications are mostly due to delayed diagnosis or treatment. The possibility of necrotizing enterocolitis (NEC) is to be considered in the differentials as it is much more common in premature neonates. MIOFI presents without peritonitis or sepsis, and the typical radiological signs of NEC such as the pneumatosis intestinalis will be absent. Spontaneous intestinal perforation is another important differential; but they do not present with prolonged or severe abdominal distension before the onset of perforation. Hirschsprung disease is uncommon in preterm babies and it can be excluded by demonstrating ganglion cells in the colonic biopsy.

CONCLUSION

Although MIOFI is an uncommon disease, its incidence is on the rise due to improved survival of extremely premature neonates. Prompt early diagnosis of MIOFI is essential for good outcome after conservative treatment. Long segment aganglionosis is a potential differential diagnosis of MIOFI.

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