An acute abdomen in a preterm infant… seems like a common enough presentation!!

Dr Pita Birch
Director of Neonatology
Mater Health, Brisbane, Australia

materhealth.org.au

1

Introduction

Director of Neonatology at Mater Hospital, Brisbane

- Mater is Australia's largest Maternity Hospital with > 10,500 births
- I have been the director there for nearly two years
- Previously in the Gold Coast, Queensland and originally from NZ

• Thank you to ICHMSI for the opportunity to speak here this morning

[Footer] 2

2

Case Example

Male infant born in ambulance on way to regional hospital

- 26 weeks, BW 750g (28th centile), APGAR 3^1 and 5^5, intubated, ECM, surfactant

Transfer to RBWH intubated and ventilated

- RDS/HMD, pneumothorax → evolving chronic neonatal lung disease – CPAP
- PDA – closed with a single course of ibuprofen
- Apnoea of prematurity – stable on Caffeine
- Anaemia of prematurity – single red blood cell transfusion
- Bilateral grade 1 IVH, no ROP

Transfer to MMH on day 43 (32 weeks CGA) with acute bowel obstruction

- Full enteral feeds established on day 10 with Pasteurised Donated Human Milk (PDHM)
- Intermittent abdominal distention = CPAP belly (tolerating feeds, stooling)
- Mild postnatal growth failure (growth dropped from 28th to below 3rd centile)
- Bovine based Human Milk Fortifier (HMF) introduced on day 31 (growth improved)
- Features of an acute abdomen on day 41
  - Abdominal distention, bile stained gastric residues, palpable mass right side abdomen

[Footer] 3

3

Differential Diagnosis and Plan

What do you think are the main differential diagnoses?

What would be your management plan?

Who would treat this baby for NEC (antibiotics, cease feeding, x-rays, call surgeons)?

YES vs NO

[Footer] 4

4

Case Example

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- Features of abdominal obstruction on day 41
  - Abdominal distention, bile stained gastric residues, palpable mass right side abdomen
- **Enteral feeds ceased, commenced antibiotics for NEC, serial abdominal x-rays**

[Footer] 5

5

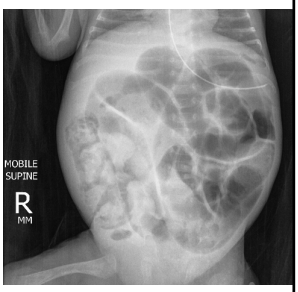
Differential Diagnosis and Plan

What are the salient features on the abdominal x-ray?

What are the classic features present?

What about now; who would treat this baby for NEC?

YES vs NO



[Footer] 6

6

Differential Diagnosis and Plan

What are the salient features on the abdominal x-ray?

What are the classic features present?

What is the most likely diagnosis?

a. Necrotising Enterocolitis
b. Intussusception
c. Milk Curd Obstruction
d. Malrotation with Volvulus

[Footer] 7

7

Case Example

Taken to theatre for laparotomy +/- bowel resection +/- stoma formation

- What did they find in theatre?

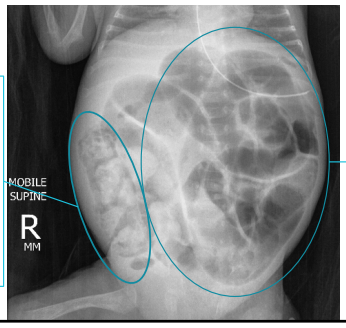
a. Widespread necrotising enterocolitis and necrotic bowel
b. Focal necrotising enterocolitis
c. Milk curd obstruction and healthy bowel
d. Volvulus and necrotic bowel

[Footer] 8

8

Worrying X-Ray Findings

Right-sided abdominal mass (intra-luminal) surrounded by a halo of air. Cannot rule out NEC / pneumatosis But this is classic for MCO



Grossly dilated bowel loops

[Footer] 9

9

Case Example

Taken to theatre for laparotomy +/- bowel resection +/- stoma formation

- Intraoperative findings
  - Milk curd obstruction at the terminal ilium
  - Fixed loop in the right iliac fossa with area of "pending perforation"
  - No evidence of necrotising enterocolitis
- Intraoperative Management
  - Luminal contents milked into the colon and out through to rectum
  - Area of impending perforation oversewed
  - No resection and no stoma required
- Postoperative Course
  - Did well post surgery
  - Remained intubated and ventilated for 2 days then extubated to CPAP
  - Nil by mouth and antibiotics for 3 days
  - Established enteral feeds without complication
  - Transferred back to RBWH on day 52 of life on full enteral feeds with PDHM (no HMF)

[footer] 10

10

Milk Curd Obstruction in Preterm Infants

Introduction

Milk Curd Obstruction Project

- Joint project between Mater Mother's Hospital and the Royal Brisbane and Women's Hospital

Mater Mother's Hospital Brisbane

- Australia's largest maternity hospital
- 10,500 births per annum
- 79 cot neonatal critical care unit
  - 2000 admissions a year
- 47 neonatal intensive care cots
- Surgical referral centre for the region
- 230-240 admissions < 32 weeks or < 1500g

Royal Brisbane and Women's Hospital

- Perinatal centre and retrieval service
- 240-250 admissions < 32 weeks or < 1500g
- Up until 2014 RBWH also surgical centre
- Home of the Queensland Milk Bank

11

11

Milk Curd Obstruction in Preterm Infants

Milk Curd Obstruction

History

- MCO described by many different names in the literature
  - Milk curd syndrome, Inspissated milk syndrome, Milk plug syndrome and Lactobezoar
- Came to prominence in the 1960s – 1970s
  - Intestinal obstruction due to milk curd first described in 1969[1]
  - Radiological findings described in 1970[2] ("Smythe's syndrome") and two cases in 1972[3]
  - Review in 1977 describes milk bolus obstruction due to cow's milk-based formula[4]
  - Formula production refined and improved to be better suited to neonatal physiology
  - Disappeared in the literature from 1980s until reappeared in the 2000s
  - Several case studies published (2000, 2002, 2003, 2009, 2012, 2013, 2014, 2017, 2019)
  - Speculation about the re-emergence of this condition is around an association with improved survival in preterm infants and widespread fortifier use

1. Cook RMC, Rickham PP. Neonatal intestinal obstruction due to milk curds. J. Ped. Surg. 1969; 1969; 599-605
2. Cremin BJ, Smythe PM, Cywes S. The radiological appearance of the "inspissated milk syndrome": a cause of intestinal obstruction in infants. Br J Radiol. 1970 Dec;43(516):856-8.
3. Friedland GW, Rush WA, Hill AJ. Smythe's "Inspissated Milk" Syndrome. Radiology. 1972 Apr 1;103(1):159–61.
4. Lewis CT, Dickson JA, Swain VA. Milk bolus obstruction in the neonate. Arch Dis Child. 1977 Jan;52(1):68–71.

12

12

Milk Curd Obstruction in Preterm Infants

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Milk Curd Obstruction

Analysis found milk curd composition to be calcium soap (salt of a fatty acid)

- Thought to be due to poor absorption of fat and calcium
- Human breastmilk fat thought to be more easily absorbable than fat found in formula
- More mature infants able to absorb the fat in modern formula
- Re-emergence of this condition due to preterm gut immaturity and poor fat absorption associate with formula designed for the high caloric needs of preterm infants
  - Up until 2009 all but one case in literature described MCO secondary to preterm formula use[1]
  - 1 case associated to HMF
- Likely to be under-recognised and when surgery is not required the condition is often diagnosed and managed as NEC[2]
- More recently associated with HMF[1] and also with previous gastrointestinal pathology, including surgery for abdominal pathology[2]

Wagener S, Cartwright D, Bourke C. Milk curd obstruction in premature infants receiving fortified expressed breast milk. J Paediatr Child Health. 2009 Apr;45(4):228–30
Maistry N, Wagener S. Milk curd obstruction: an increasingly common rarity? J Clinical Neonatology 2019; 8(4): 212-215

13

13

Milk Curd Obstruction in Preterm Infants

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Milk Curd Obstruction

MCO in Brisbane

- In 2009 our group described 9 infants with MCO[1]
  - 9 infants from 2001 to 2007, all had MCO associated with fortification of EBM
    - Still a rare condition: rate of 3.4 per 1,000 preterm infants < 31 weeks gestation
    - At the time 80% of infants < 31 weeks had received EBM (nearly all fortified)
    - 4 (44%) died prior to discharge – 2 died of sepsis following surgery, 2 died several months later of respiratory disease
    - 4 had previous abdominal surgery (meconium ileus, ileostomy for NEC, 2x surgery for SIP)
  - HMF does **not** have extra fat but does contain extra calcium
  - High calcium can cause fat malabsorption
  - Does the high calcium content in HMF (and preterm formula) impair fat absorption and subsequently result on milk curd soap formation and MCO?
  - Is there a relationship to previous abdominal pathology/surgery and MCO?
  - Suspect that MCO is underrepresented – misdiagnosed and treated as NEC
    - Rare condition that is not commonly considered
    - Conservative management may lead to resolution of both conditions

Wagener S, Cartwright D, Bourke C. Milk curd obstruction in premature infants receiving fortified expressed breast milk. J Paediatr Child Health. 2009 Apr;45(4):228–30

14

14

Milk Curd Obstruction in Preterm Infants

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MCO in Brisbane (part 2)

Repeat of the 2009 Case Series (PI, Dr Jasmine Antoine)

- Since 2009 series HMF use in RBWH dropped dramatically, whilst MMH maintains a nearly 100% fortifier use in preterm infants < 32 weeks
- Clinical study of cases of MCO from 1st January 2008 until 1st November 2019
  - Rate of MCO in preterm population of Brisbane
  - Relationship with feeding, including any nutritional additives
  - Presenting symptoms, management and outcomes
- Only preliminary data from RBWH collected
  - 17 cases of MCO diagnosed, mean gestational age 26 weeks (range 23 – 31)
  - 9 (53%) required surgical intervention; 8(47%) managed conservatively, all survived to discharge
  - 10 (59%) developed MCO associated with HMF use
  - 4 (29%) received formula (preterm or term formula)
  - 3 (18%) did not receive HMF or formula, but all 3 received phosphate supplementation
  - Mean day of onset 44.9 days of age (range 22 – 98 days)
  - When associated with HMF use mean onset 28 days after fortification (range 2 – 83 days)

[Footer]

15

15

Milk Curd Obstruction in Preterm Infants

Summary

What we know?

- MCO is a real entity described since 1969
  - Initially associated with formula use, but disappeared from literature in 1980
  - There has been a re-emergency in the literature since 2000
- MCO caused by soap formation
  - A calcium-fatty acid soap forms in the small bowel, usually obstructing in the distal small bowel (ileocecal junction)
- MCO is an important cause of neonatal bowel obstruction in preterm infants
  - Recent literature reports are almost exclusively in preterm infants
  - Radiological feature is of a right sided intraluminal mass surrounded by an air halo
  - Conservative (non-operative) management can be effective
    - Previous reports showing a very high rate of surgical management probably represents under-reporting where the diagnosis is only made at time of surgery
  - Surgical management includes "milking" of MCO out of bowel, but can require intestinal surgery (resection, stoma formation, primary anastomosis)

16

Milk Curd Obstruction in Preterm Infants

Summary

What we think we know?

- MCO is likely to be under-diagnosed
  - Diagnosed and treated as NEC
  - Diagnosis may only be made when infant undergoes surgery
    - In a unit with a very high level of vigilance for this condition, early recognition and conservative management is possible
- MCO is associated with previous surgery and/or previous abdominal pathology
  - Previous pathology may increase risk of soap formation **and/or** increase risk of the soap/curd obstructing the bowel

What we can speculate?

- MCO in preterm infants may be associated with bovine-derived HMF, bovine formula or possibly phosphate supplementation
  - Any association with phosphate use not been previously reported
- Will human-derived HMF protect against MCU or will the association be similar?

17

Milk Curd Obstruction in Preterm Infants

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- Dr Jasmine Antoine, Neonatologist, RBWH
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- Dr Chris Bourke, Surgeon, QCH

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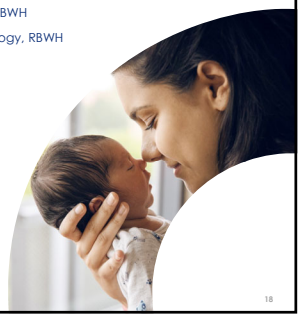
- Prolacta Bioscience

- Disclaimer:
  - Prolacta Bioscience has supported me to attend ICHMS 2020
  - The content of this presentation has been developed independently of Prolacta Bioscience



18