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Metabolic Bone Disease of Infancy in the Offspring of Mothers With Bariatric Surgery: A Series of 5 Infants in Contested Cases of Child Abuse

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Original article

Metabolic Bone Disease of Infancy in the offspring of mothers with bariatric surgery: A series of 5 infants in contested cases of child abuse

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SUMMARY

Background and aims: Metabolic Bone Disease of Infancy is a multifactorial disorder of bone fragility in infants who typically present under 6 months of age with multiple unexplained fractures. Major risk factors for this disorder relate to the fetal time period and include decreased provision of the essential nutrients for bone formation during pregnancy (calcium, phosphate, vitamin D, and protein), prematurity, and decreased fetal bone loading.
Methods: This study presents 5 infants with multiple unexplained fractures born to women who had prior bariatric surgery in which child abuse was alleged, and the alleged perpetrator denied wrong doing.
Results: The radiographic findings showed poor bone mineralization and were consistent with Metabolic Bone Disease of Infancy.
Conclusions: Using the Utah Paradigm to understand risk factors for MBDI, the authors believe the nutritional deficiencies that accompany bariatric surgery likely contribute to the bone fragility in these 5 infants. Other risk factors for MBDI were appreciated in 4 of the 5 cases. 1,25 dihydroxyvitamin D was elevated or high-normal suggesting calcium deficiency in 2 cases. We believe infants born to mothers who have had prior bariatric surgery are at increased risk for bone fragility and MBDI during the first 6 months of life.

1. Introduction

Metabolic Bone Disease of Infancy (MBDI) is a recently described multifactorial disorder of bone fragility in which young infants under 12 months of age (most under 6 months of age) present with multiple unexplained fractures (MUF) [1]. The radiographic findings, risk factors, and lab studies of MBDI are helpful in establishing this diagnosis and distinguishing it from child abuse. One of the risk factors for MBDI is decreased provision of the essential nutrients for bone formation and mineralization (calcium, phosphate, vitamin D, and protein) during pregnancy, especially the third trimester.

Morbidly obese patients are increasingly having bariatric surgery for weight loss. Bariatric surgery in the USA is typically one of 2 procedures - Roux-en-Y gastric bypass surgery (RYGBS) and gastric sleeve surgery (GSS) [2]. RYGBS results in the surgical removal of the lower portion of the stomach leaving the remaining small, upper portion of the stomach (the pouch) as the chamber that accepts food from the esophagus. The pouch is then connected to the jejunum and thus bypasses the duodenum. GSS removes about 80% of the stomach leaving the chamber that accepts from the esophagus significantly reduced. In the gastric sleeve there is no intestinal bypass of gastric contents.

Individuals who have bariatric surgery often have both protein-calorie and micronutrient deficiencies that can have adverse consequences on bone metabolism leading to reduced bone strength [2–8]. Women who have had bariatric surgery, either RYGBS or GSS, are thus at increased risk for not being able to provide the fetus with sufficient protein-calories and essential micronutrients for normal growth and for normal bone formation. Thus, not unexpectedly, there is an increased risk for intrauterine growth retardation in the offspring of women who have had bariatric surgery [9,10]. Because the rapidly growing skeletal system of the third trimester fetus requires sufficient calcium, phosphate, vitamin D, and protein for attaining normal fetal bone strength, the fetus of a pregnant mother who has had bariatric surgery is at increased risk

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for diminished bone strength and at an increased risk for fragility fractures once born.

Herein we describe 5 cases of infants with MBDI in which child abuse was diagnosed. The mothers had prior bariatric surgery, and we believe this is yet another risk factor for MBDI as a result of the nutrient deficiencies associated with bariatric surgery.

2. Methods

We are asked to do forensic review cases of infants with MUF in which child abuse has been diagnosed, and the alleged perpetrator denies wrongdoing in order to determine if there might be a plausible medical explanation for the fractures.

In a recent 12 month period we reviewed 4 cases of infants with MUF in which the mother had bariatric surgery prior to her pregnancy (3 pregnancies; one set of twins in which both were affected). We also appreciated there was one infant with MUF prior to this time period.

We evaluated the radiographs in these 5 infants for the radiographic findings of MBDI (healing rickets) that include the following [1]:

1. **Periosteal Mineralization Abnormality.**
2. **Growth Plate Mineralization Abnormality.**
3. **Ulnar cupping.**
4. **Skull Mineralization Abnormality.**
5. **Rib Mineralization Abnormality.**
6. **Vertebral Mineralization Abnormality.**
7. **Looser Zones.**
8. **Osteopenia.**

The clinical histories were evaluated for known risk factors for MBDI, and laboratory findings were also evaluated for abnormalities suggesting MBDI.

The study was approved by the Dayton Children's Hospital IRB.

3. Results

3.1. Case vignettes

A brief summary of the 5 cases follows:

3.2. Case 1 (male)

He was the 3210 g product of a term pregnancy and vaginal delivery. Fetal movement was normal. Mother's medical history is significant for a RYGBS 5 years prior to the birth of infant. Mother's 25 hydroxyvitamin D (25OH-VD) levels prior to delivery were:

1. 15 months prior to delivery = 15 ng/ml (NORMAL 30–100).
2. 12 months prior to delivery = 38 ng/ml (NORMAL 30–100).

During the pregnancy mother was prescribed PrenaPlus tablets - 1 per/day and Vitamin D - 10,000 IU/day, and iron - 65 mg/day. She often did not take these medications.

At 5 weeks of age mother noted a RIGHT leg limp immediately after a diaper change. Upon admission to the hospital, the following were noted:

1. Skeletal Survey:
   a. Classical Metaphseal Lesion (CML) of distal RIGHT femur and probable fracture of the proximal RIGHT tibia.
   b. Irregularity of distal metaphysis of LEFT ulna, concerning for a fracture.
   c. Irregularity of medial metaphysis of distal LEFT femur, concerning for fracture.
   d. Diffuse periosteal reaction along the shafts of the RIGHT humerus, LEFT humerus, RIGHT femur, LEFT femur, worrisome for healing injuries.
2. Skin exam showed no bruising.
3. Blood studies:
   a. Calcium = 10.3 mg% (NORMAL = 9–11).
   b. PTH intact = 47 pg/ml (NORMAL = 15–65).
   c. 25OH-VD = 31 ng/ml (NORMAL > 20).
   d. 1,25 dihydroxyvitamin D (1,25 diOH-VD) = 145 pg/ml (NORMAL: 15–75).
4. Blood studies on mother at the time of the infant fractures showed:
   a. Calcium = 9.5 mg%.
   b. PTH = 55 pg/ml.
   c. 25OH-VD = 51 ng/ml (NORMAL > 20).
   d. 1,25 diOH-VD = 122 pg/ml (NORMAL: 15–75).
   e. Phosphate = 3.8 mg% (NORMAL: 4.0–5.7).

Physical examination by author MEM was normal 2 days after the fractures were appreciated.

Child abuse was diagnosed and the parents denied wrongdoing. There are 2 other older siblings who were thriving at home. After legal proceedings the infant was returned to the parents.

3.3. Case 2 (female)

She was the 2624 g product of a 39 2/7 week pregnancy and precipitous vaginal delivery. Mother has a bicornuate uterus, and at the time of delivery she was in the breech presentation in the RIGHT horn of the bicornuate uterus. She was diagnosed with SGA (small for gestational age).

Mother had a history of morbid obesity and had a RYGBS at age 28, 4 years prior to delivery. During the pregnancy she was prescribed both a calcium and Vitamin D supplement which she did not take.

Mother's 25OH Vitamin D level 5 weeks after delivery was 23 ng/ml [NORMAL: 30–100].

At 10 weeks of age she was fussy, and mother noted a “clicking” in the LEFT side of the chest. Previously the 2 year old brother was playing with her and may have fallen on her. A chest X-ray showed LEFT sided rib fractures. She was admitted to the hospital where the following were done/noted:

1. Skin exam showed no bruising.
2. Skeletal survey:
   a. LEFT-sided acute postero-medial rib fractures: 6-8.
   b. LEFT-sided acute antero-lateral rib fractures: 5-7.
   c. Healing LEFT postero-medial fracture of rib 8.
   d. Acute fracture of the LEFT 5th metacarpal.
   e. Subtle asymmetric sclerosis of the distal metaphysis of the LEFT radius.
3. Blood studies:
   a. Calcium = 9.8 mg% (NORMAL: 8–11).
   b. Alkaline phosphatase = 478 U/L (NORMAL: 126–610).
   c. 25OH-VD = 37 ng/ml (NORMAL: 30–100).
   d. PTH = 56 pg/ml (NORMAL: 6–88).
4. Head CT scan: Normal.
5. Eye exam: No retinal hemorrhages.

Mother was diagnosed with the hypermobile type of Ehlers Danlos Syndrome (h-EDS).

Child abuse was alleged, and parents denied wrongdoing.

3.4. Case 3 (male)

He was the 3475-g product of a 38-week pregnancy and repeat Cesarean delivery. Mother noted decreased fetal movement in 3rd trimester which the mother noted to her obstetrician and was thus followed with serial ultrasound examinations. Mother took prenatal vitamins, Ranitidine 150 mg BID po for heartburn during most of the pregnancy, and Magnesium oxide 400 mg BID po for migraines.

Mother had a history of obesity and had a RYGBS at age 28, 4 years prior to delivery. Because of the RYGBS, mother also took 5000 units of Vitamin D/day and received iron infusions for anemia. Mother had multiple episodes of reactive hypoglycemia during the pregnancy.

Placenta examination showed an umbilical cord length = 17 cm (Normal: 50–60 cm for term infant).

A**t 9 weeks of age** father found the infant had fallen out of his swing (14-inch fall) and noted his head was swollen. He was admitted to the hospital for 3 days where the following was done/noted:

1. Skeletal Survey 9/3/2019:
   a. Healing LEFT 6th rib posterior fracture.
   b. Healing fractures of RIGHT ribs 5-7.
2. Head CT Scan:
   a. Subdural or epidural hematoma of LEFT parietal brain measuring 3 mm.
   b. LEFT parietal bone fracture.
   c. LEFT parietal scalp hematoma.
3. Normal cervical spine X-rays.
4. Blood Studies:
   a. Calcium = 10.1 mg% (NORMAL: 8.8–10.8).
   b. Phosphate = 6.2 mg% (NORMAL: 4.8–7.4).
   c. 25OH-VD = 28 ng/ml (NORMAL: >30).
   d. PTH = 11 pg/ml (NORMAL: 18–88).
   e. 1,25 diOH-VD = 75 pg/ml (NORMAL: 15–75).

Child abuse was diagnosed, and parents denied wrongdoing.

3.5. Cases 4-A and 4-B (Twins)

Twin A - female was the 2480 g and Twin B - male was the 2170 g product of a 38 1/7 week twin pregnancy and Cesarean delivery for malpresentation born on 3/7/2019 to a 33 year old mother. Both were SGA, and Twin A was in the breech presentation.

Mother had a GSS approximately 6 months prior to becoming pregnant with the twins and lost 50 pounds during fertility treatment. One year prior to becoming pregnant mother's 25OH-VD level was 11 ng/ml, and 3 months after delivery was 20 ng/ml (NORMAL 30–100).

Mother was on antacids during the pregnancy for treatment of heartburn.

Placenta examination showed markedly short umbilical cords:

Twin A = 7.5 cm.
Twin B = 23.7 cm.
(NORMAL: 50–60 cm for term pregnancy).

They were breast fed with vitamin D supplementation.

At **9 weeks of age** Twin B was diagnosed with GERD and atopic dermatitis and started on Zantac. There were multiple formula changes because of feeding difficulties.

At 12 weeks of age parents thought the RIGHT testicle of Twin B was swollen and sought medical attention. Medical evaluation showed the RIGHT testicle to be normal, but his LEFT forearm was swollen. The following were done/noted:

1. Skeletal survey:
   a. Healing LEFT posterior 7th rib fracture with callus.
   b. Healing LEFT lateral 4th and 5th rib fractures.
   c. Healing RIGHT anterior 3–7 rib fractures.
   d. Subacute fractures of LEFT radius and ulna.
2. Blood studies:
   a. Calcium = 10.0 mg% [NORMAL: 7.8–11.3].
   b. Phosphate = 5.8 mg% [NORMAL: 4.8–8.2].
   c. Alkaline Phosphatase = 371 U/L [NORMAL: 70–345].
   d. Osteogenesis Imperfecta - 3 Gene Panel: NORMAL.

The parents had no explanation for the MUF, and child abuse was being considered. This prompted an immediate evaluation of Twin A.

At 5 weeks of age Twin A was started on Zantac for vomiting and feeding difficulties.

At 12 weeks of age Twin A was evaluated because of Twin B's MUF where the following were done/noted:

1. Skeletal survey:
   a. Healing RIGHT anterolateral 2–6 rib fracture with callus.
   b. Healing LEFT anterior 3–5 rib fractures
   c. Subtle irregularity of LEFT proximal fibula.
   d. Physiologic periosteal new bone formation.
2. Blood studies:
   a. PTH = 38.4 pg/ml [NORMAL: 12–65].
   b. 25OH-VD = 27 ng/ml [NORMAL: >20].
   c. Osteogenesis Imperfecta - 3 Gene Panel: NORMAL.

Child abuse was alleged, and parents denied wrongdoing. After legal proceedings the twins were returned to their parents.

4. Results

Table 1 summarizes the clinical, radiographic, and lab studies in the 5 cases. There were 4 or more rib fractures in 4 of the 5 infants. CMLs were noted in 2 infants.

Table 2 summarizes the 8 radiographic abnormalities we evaluated in each case. As previously noted, we believe the diagnosis off MBDI can be made if one or more of these 8 abnormal X-ray findings is found. Table 2 indicates each case had multiple abnormal radiographic findings, thus establishing the diagnosis of MBDI in each infant: 2 infants had 4 radiographic abnormalities and 3 infants had 5. Moreover, several risk factors for MBDI were found in each of the 5 infants providing additional support for this diagnosis:

   a. Maternal h-EDS.
   b. Decreased fetal bone loading in 2.
   c. SGA in 3.
   d. Drugs that affect bone quality in 3.
   e. Twins in 2 (twins also have decreased fetal bone loading as well as a greater challenge for mother to transfer essential bone nutrients during the pregnancy compared to a singleton pregnancy).

In Case 1 there was a markedly elevated 1,25 diOH-VD in both the infant and mother, and in Case 3 the infant had a high normal value. Elevated 1,25 diOH-VD causes increased bone resorption, and thus increases bone fragility [1,20].

Fig. 1 shows examples of the radiographic abnormalities of MBDI found in the 5 infants.

Table 1
Clinical findings in 5 cases of infants with multiple fractures born to mothers with bariatric surgery.

Case (M/F)	Type BS	BW (gms)	GA (wks)/ Del	Age Pr Fxs (wks)	# Fxs Types Fxs	# Rib Fxs	Inf[a] 25VD ng/ml	Inf[b] 1,25 VD pg/ml	Mat[a] 25VD ng/ml	Mat[b] 1,25VD pg/ml	Inf Ca	Inf P	Other MBDI Risk Factors
1. M	RYGBS	3210	40 VaD	5	8 4 CMLs 4 SPNBF	0	31	145	15 38	122	N	N	Probable VDD
2. F	RYGBS	2624	39 VaD	10	8 6 acute rib 1 healing rib 1 metacarpal	7	37	ND	23	ND	N	ND	DFBL: Breech and Bicornuate Uterus SGA h-EDS
3. M	RYGBS	3475	38 CS	9	4 healing rib	4	28	75	ND	ND	N	L	DFBL Drugs: Zantac, Mg
4-A F	GSS	2480	38 CS	12	11 8 healing rib CML 2 SPNBF	8	27	ND	11 20	ND	ND	ND	Twin SGA Drugs: Antacids
4-B M	GSS	2170	38 CS	12	10 8 healing rib LEFT ulna and radius	8	ND	ND	11 20	ND	N	N	Twin SGA Drugs: Antacids

Abbreviations: M = Male, F = Female, BS = Bariatric Surgery, RYGBS = Roux-En-Y Surgery, GSS = Gastric Sleeve Surgery, GA = Gestational Age, Del = Delivery type, VaD = Vaginal Delivery, CS = Cesarean Delivery, Age Pr Fxs = Age of Presentation With Fractures, VD = Vitamin D, Inf = Infant, Mat = Maternal, Ca = blood calcium, P = blood phosphate, ND = Not Done, N = Normal, L = Low, VDD = Vitamin D Deficiency, DFBL = Decreased Fetal Bone Loading, SGA = Small for Gestational Age, h-EDS-type 3 = Ehlers Danlos Syndrome, hypermobile type, SPNBF = Subperiosteal New Bone Formation. The Table shows findings in these 5 cases that are typical of MBDI [1]:
a. In 4 infants there were 4 or more rib fractures without severe internal thoracic injury and without severe respiratory distress, a finding that indicates these are fragility fractures.
b. The narrow range of presentation typically within the first 3 months of life (range: 5–12 weeks) suggests fetal factors are likely the basis of the fragility fractures.
c. The high 1,25diOH- VD levels in Cases 1 and 3 are consistent with insufficient total body calcium [1,20].
d. There were risk factors for MBDI other than the maternal bariatric surgery. In CASE 1 there was only possible VDD, likely from the sequelae of the bariatric surgery. In the other 4 cases there was DFBL. Both bicornuate uterus and breech presentation are associated with DFBL from intrauterine confinement. Twins always have DFBL because of the intrauterine confinement of twice the fetal volume in the same maternal uterine volume. Maternal administration of drugs during pregnancy that affect bone quality and strength were present in 3 cases. One mother had h-EDS 3.
e. Radiologists will often mistakenly call CMLs and SPNBF fractures, whereas these two findings are often indicative of MBDI [1,32,33].
[a] 25 VD: Normal = 30–100 ng/ml.
[b] 1,25 VD: Normal = 15–75 pg/ml.

Table 2
MBDI radiographic abnormalities in 5 young infants with multiple fractures born to mothers who had gastric bypass.

MBDI Radiographic Abnormality	Case 1	Case 2	Case 3	Case 4 Twin A	Case 4 Twin B
1. SPNBF	+	−	−	+	−
2. Growth Plate Mineralization Abnormality	+	+	+	+	+
3. Ulnar Cupping	−	−	−	−	+
4. Skull Mineralization Abnormality	−	+	+	−	−
5. Vertebral Mineralization Abnormality	−	+	+	+	+
6. Rib Mineralization Abnormality	+	+	−	+	−
7. Looser Zones	−	−	+	−	+
8. Osteopenia	+	−	+	+	+

+ = Present − = Absent.
Table 2 summarizes MBDI the 8 radiographic findings of MBDI (healing rickets) in each of the 5 cases. There were 2 infants who had 4 findings and 3 infants who had 5 findings.

5. Discussion

5.1. MBDI and the Utah Paradigm

The multifactorial causation of MBDI is readily understood through the Utah Paradigm [1,11]. MBDI is a bone fragility disorder that typically presents in the first 6 months of life with MUF and is often misdiagnosed as child abuse.

Newborn and young infant bone strength is determined by the adequate provision of essential nutrients for development of normal bone strength including protein, vitamin D, calcium, and phosphate during the third trimester, as well as sufficient bone loading during the third trimester [1]. Any situation that causes decreased fetal bone loading or compromises these essential nutrients needed for normal fetal bone formation will increase the risk for young infant fragility fractures and MBDI. Such a presentation of an infant with MUF could be confused for child abuse.

5.2. Consequences of bariatric surgery on fetal bone development and strength

Women who have had bariatric surgery and become pregnant may be unable to provide the essential nutrients needed to produce normal fetal bone strength. Both RYGBS and GSS result in absorption of fewer calories and nutrients [3–8]. Vitamin D and calcium are primarily absorbed in the duodenum, and phosphate is absorbed in the duodenum as well as the jejunum. Thus, gut physiology in individuals who have had RYGBS, in which the duodenum is bypassed, is very unfavorable for providing essential micronutrients for normal fetal bone formation. RYGBS is especially unfavorable for providing adequate calcium in a pregnant woman as calcium absorption is additionally compromised by the lower acid content of the gut. Calcium is best absorbed in an acid environment, and because much of the stomach that generates acid is removed in the RYGBS, patients that undergo this procedure need to take a calcium supplement as well as vitamins [12].

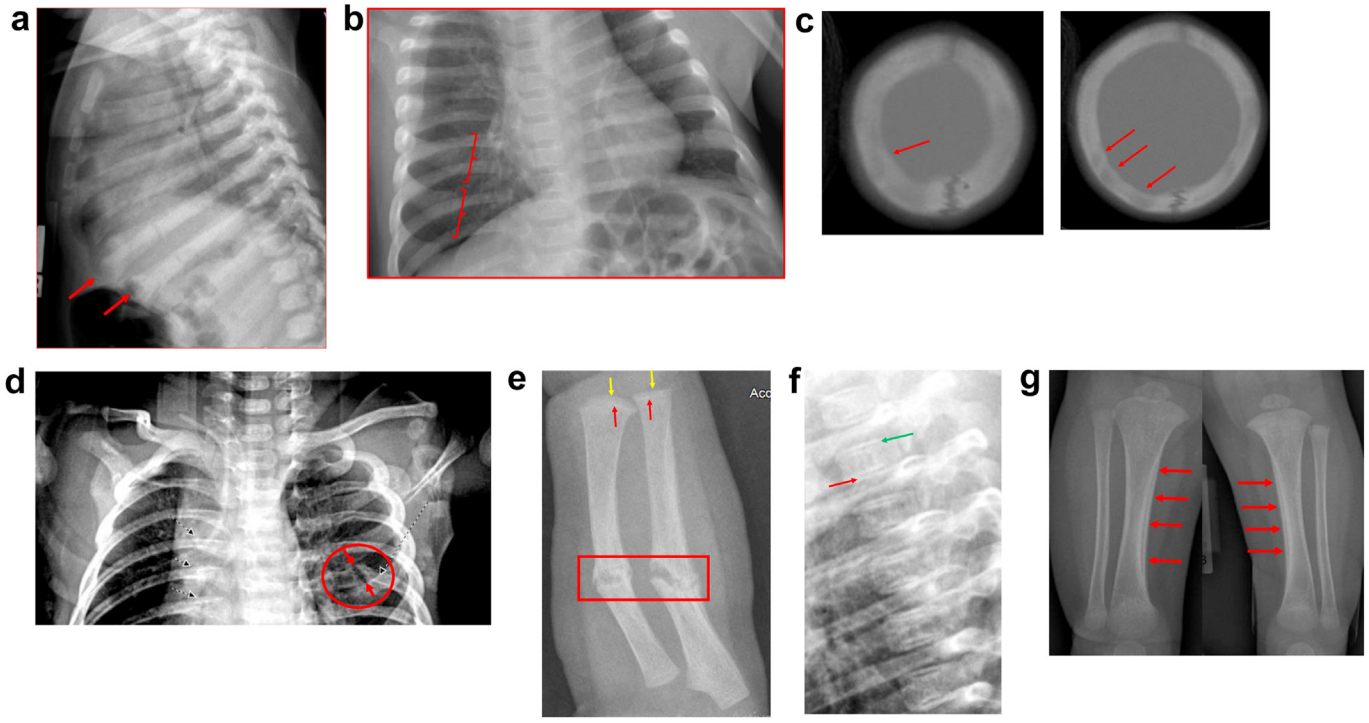

Fig. 1. Radiographic Examples of MBDI.
a: CASE 2. The lateral chest X-ray shows cupping of the ribs (red arrows). This finding is consistent with a rachitic rosary and MBDI [1].
b: CASE 4-A. The AP chest shows widened ribs at the costochondral junction (red brackets) as a result of accumulation of nonmineralized osteoid. This finding is consistent with a rachitic rosary and MBDI [1].
c: CASE 2. Two of the head CT axial images are shown above. Normally the skull should be homogeneously mineralized throughout its entirety. However, there are multiple regions of spherical defects consistent with poorly mineralized bone. This is consistent with craniotabes and MBDI [1].
d: CASE 3. The chest radiograph shows a Looser Zone of the rib (red circle). The apparent rib fracture has an oblique seam of dark in between whiter, calcified rib. The dark seam is nonmineralized bone, consistent with a Looser Zone and MBDI [1].
e: CASE 4-B. The LEFT forearm shows wide seams of nonmineralized bone in both the ulna and radius, perpendicular to the long axis of each bone (red rectangle). The margins are sclerotic and consistent with a Looser Zone and MBDI [1]. At the distal end the ulna and radius the normal zone of provisional calcification (ZPC) is shown by the yellow arrows. Beneath this ZPC, however, a second ZPC is shown by the red arrows. The region between the two ZPCs is a rachitic intermediate. This finding is consistent with MBDI [1].
f: CASE 3. All of the vertebral bodies in this lateral view of the spine show a "bone-in-bone" appearance. Normally there is a single line of calcification outlining each vertebral body endplate. However, each endplate has 2 distinct mineralization lines (arrows) separated by a radiolucent zone. Between these 2 lines at top and bottom is a radiolucent band of nonmineralized bone. This finding is consistent with MBDI [1].
g: CASE 4-A. Radiograph of the lower legs shows bilateral symmetric SPNBF (red arrows). The thin dark band sandwiched between the cortical bone and the thin outer calcified line is nonmineralized osteoid. There is osteopenia and curvatures of the mid fibulas and distal tibiae. These findings indicate poor bone mineralization and are consistent with MBDI [1].

Long term follow-up studies of women who have had bariatric surgery show compromised bone health with decreased bone density, decreased total body calcium, VDD, and hyperparathyroidism [13–16].

Micronutrient deficiencies that result from bariatric surgery that have been reported in the literature include deficiencies in vitamin D, vitamin K, thiamine, vitamin A, folate, vitamin B12, calcium, copper, zinc, and iron. Protein deficiency can also result from bariatric surgery [2–7].

These micronutrient and protein-calorie deficiencies are the likely cause of the increased frequency of intrauterine growth retardation in babies born to mothers who have had bariatric surgery [9,10]. Bone growth is thus diminished, and thus likely bone strength.

Some individuals who undergo bariatric surgery develop severe metabolic bone disease with osteomalacia [17]. These individuals improve only with high doses of daily ergocalciferol and high doses of daily calcium. Thus for some individuals bariatric surgery can be a challenge for maintaining bone health. Even with large dose supplements, calcium and vitamin D absorption are often markedly decreased leading to deficiencies of these 2 critical micronutrients for bone formation.

Copper deficiency is another micronutrient deficiency that often results from RYGBS [18]. The copper-dependent enzyme lysyl oxidase is critical in cross-linking type 1 collagen in bone, and thus copper deficiency may also contribute to the impairment of fetal bone health in pregnant women who have had gastric bypass.

Thus, a pregnant women who has had bariatric surgery, who herself, is likely deficient in essential nutrients for her own bone health, may be at a significant disadvantage in her ability to provide these essential nutrients to the fetus to promote normal fetal bone mineralization and strength, a warning that has been published in the bariatric literature [19]. The elevated 1,25 diOH-VD testing in the mother and infant of CASE 1 and the high normal result in the infant of CASE 3 are consistent with insufficient total body calcium in these 2 infants and in the mother [20]. Thus it is reasonable to conclude bariatric surgery is a risk factor for MBDI.

Sempos has recently presented a multivariate analysis that demonstrates a low calcium diet coupled with low 25OH vitamin D levels is synergistic in promoting nutritional rickets [21].

5.3. Other MBDI risk factors in the 5 cases

MBDI is multifactorial in causation, and fetal risk factors for MBDI other than maternal bariatric surgery were present in 4 of these 5 infants (Cases 2–5). The mother of Case 1 likely had VDD

during the pregnancy, and in Case 1 the bariatric surgery may be the only risk factor for MBDI.

Decreased fetal bone loading will lead to decreased fetal/newborn bone strength. Fetal movement is the primary cause of fetal bone loading as the fetal body hits the maternal uterus [1]. Umbilical cord length is directly related to the extent of fetal movement in the third trimester [22]. In Cases 3, 4-A, and 4-B there was a very short umbilical cord, and in Case 3 mother complained to her obstetrician of decreased fetal movement. Cases 4-A and 4-B were twins.

Quantitative ultrasound speed of sound (SOS) measurements of the tibia in newborns with short umbilical cords are also slower compared to those with normal length umbilical cords [23,24].

Quantitative ultrasound speed of sound (SOS) measurements of the tibia in newborn twins are slower than those in singletons indicating less favorable bone quality (and thus lower bone strength) in twins compared to singletons [25].

Twins are at increased risk for MBDI compared to singleton pregnancies because of the intrauterine confinement leading to decreased fetal bone loading, and the greater challenge for the mother to provide essential nutrient for bone to two fetuses as opposed to one fetus [1,26].

Drug exposures during pregnancy are another risk factor for MBDI, and the mother of CASE 3 was on chronic Zantac and magnesium. Zantac is an acid lowering drug that causes decreased calcium absorption and magnesium has a direct effect on bone quality and decreases bone strength [27–29].

Infants who have intrauterine growth retardation (aka SGA) are another risk factor for MBDI as they have lower bone strength compared to normal birth weight babies [30]. As previously noted, there is an increased frequency of SGA infants in the offspring of mothers who have had bariatric surgery [8,9]. In the present series 3 of the 5 infants were SGA.

h-EDS has also been shown to be a risk factor for MBDI [1,31].

5.4. Observations that child abuse is unlikely in these 5 cases

Noteworthy, 4 of the 5 infants in this series had 4 or more rib fractures without any internal thoracic injury or sever respiratory distress. Garcia found that whenever a child had 4 or more rib fractures from a high force accident (motor vehicle accident, pedestrian accident, or violent child abuse) there was severe internal thoracic injury and severe respiratory distress [32]. Applying the conclusion of the Garcia study to these 4 cases would strongly indicate these are fragility fractures, possibly from the physical forces of the birthing process. The lack of bruising in these cases is also consistent with the fractures being fragility fractures [33]. While the reading radiologists interpreted CMLs and SPNBF as being specific for child abuse, these findings are far more likely to be indicative of MBDI [1,34,35].

6. Conclusion

Pregnant women who have had bariatric surgery are at increased risk for not being able to provide the essential nutrients needed for normal fetal bone mineralization. This results in decreased newborn and young infant bone strength and an increased risk for fragility fractures in the immediate postnatal period. We believe that this is yet one more risk factor for MBDI and that such an infant could be mistakenly diagnosed as a victim of child abuse.

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None.

Contribution of each author

a. **Marvin Miller:** Designed study; Reviewed the clinical information; Wrote original draft; Approved final version.
b. **David Ayoub:** Interpreted the radiographs; Approved final version.

Declaration of competing interest

a. Marvin Miller has no conflict of interest.
b. David Ayoub has no conflict of interest.

References

[1] Miller ME, Stolfi A, Ayoub D. Findings of metabolic bone disease in infants with unexplained fractures in contested child abuse investigations: a case series of 75 infants. J Pediatr Endocrinol Metabol 2019;32:1103–20.
[2] Saltzman E, Philip Karl J. Nutrient deficiencies after gastric bypass surgery. Annu Rev Nutr 2013 Jul 17;33:183–203.
[3] Verger EO, Aron-Wisnewsky J, Dao MC, Kayser BD, Oppert JM, Bouillot JL, et al. Micronutrient and protein deficiencies after gastric bypass and sleeve gastrectomy: a 1-year follow-up. Obes Surg 2016 Apr 1;26(4):785–96.
[4] Bal BS, Finelli FC, Koch TR. Origins of and recognition of micronutrient deficiencies after gastric bypass surgery. Curr Diabetes Rep 2011 Apr 1;11(2):136–41.
[5] Bal BS, Finelli FC, Shope TR, Koch TR. Nutritional deficiencies after bariatric surgery. Nat Rev Endocrinol 2012 Sep;8(9):544.
[6] Toh SY, Zarshenas N, Jorgensen J. Prevalence of nutrient deficiencies in bariatric patients. Nutrition 2009 Nov 1;25(11–12):1150–6.
[7] Liu C, Wu D, Zhang JF, Xu D, Xu WF, Chen Y, et al. Changes in bone metabolism in morbidly obese patients after bariatric surgery: a meta-analysis. Obes Surg 2016 Jan 1;26(1):91–7.
[8] Schafer AL. Vitamin D and intestinal calcium transport after bariatric surgery. J Steroid Biochem Mol Biol 2017 Oct 1;173:202–10.
[9] Adams TD, Hammoud AO, Davidson LE, Laferrère B, Fraser A, Stanford JB, et al. Maternal and neonatal outcomes for pregnancies before and after gastric bypass surgery. Int J Obes 2015 Apr;39(4):686–94.
[10] Nørgaard LN, Gjerris AC, Kirkegaard I, Berlac JF, Tabor A. Danish Fetal Medicine Research Group. Fetal growth in pregnancies conceived after gastric bypass surgery in relation to surgery-to-conception interval: a Danish national cohort study. PLoS One 2014 Mar 21;9(3):e90317. Bypass surgery. International journal of obesity. 2015 Apr;39(4):686-694.
[11] Frost HM. From Wolf's law to the Utah paradigm: insights about bone physiology and its critical application. Anat Rec 2001;262:398–419.
[12] Schafer AL, Weaver CM, Black DM, Wheeler AL, Chang H, Szefc GV, et al. Intestinal calcium absorption decreases dramatically after gastric bypass surgery despite optimization of vitamin D status. J Bone Miner Res 2015 Aug;30(8):1377–85.
[13] Cook FJ, Khanna I, Giordano J, Matarese L, Hudson S. Long-term bone health after Roux-en-Y gastric bypass: a pilot study. Endocr Pract 2017 Sep;23(9):1077–84.
[14] Lindeman KG, Greenblatt LB, Rourke C, Bouxsein ML, Finkelstein JS, Yu EW. Longitudinal 5-year evaluation of bone density and microarchitecture after Roux-en-Y gastric bypass surgery. J Clin Endocrinol Metabol 2018 Nov;103(11):4104–12.
[15] Karefylakis C, Näslund I, Edholm D, Sundbom M, Karlsson FA, Rask E. Vitamin D status 10 years after primary gastric bypass: gravely high prevalence of hypovitaminosis D and raised PTH levels. Obes Surg 2014 Mar 1;24(3):343–8.
[16] Johnson JM, Maher JW, DeMaria EJ, Downs RW, Wolfe LG, Kellum JM. The long-term effects of gastric bypass on vitamin D metabolism. Ann Surg 2006 May;243(5):701.
[17] Al-Shoha A, Qiu S, Palnitkar S, Rao D. Osteomalacia with bone marrow fibrosis due to severe vitamin D deficiency after a gastrointestinal bypass operation for severe obesity. Endocr Pract 2009 Sep 1;15(6):528–33.
[18] Gletsu-Miller N, Broderius M, Frediani JK, Zhao VM, Griffith DP, Davis SS, et al. Incidence and prevalence of copper deficiency following roux-en-y gastric bypass surgery. Int J Obes 2012 Mar;36(3):328–35.
[19] Costa MM, Belo S, Souteiro P, Neves JS, Magalhães D, Silva RB, et al. Pregnancy after bariatric surgery: maternal and fetal outcomes of 39 pregnancies and a literature review. J Obstet Gynaecol Res 2018 Apr;44(4):681–90.
[20] Lieben L, Masuyama R, Torrekens S, Van Looveren R, Schrooten J, Baatsen P, et al. Normocalcemia is maintained in mice under conditions of calcium malabsorption by vitamin D–induced inhibition of bone mineralization. J Clin Invest 2012 May 1;122(5):1803–15.
[21] Sempos CT, Durazo-Arvizu RA, Fischer PR, Munns CF, Pettifor JM, Thacher TD. Serum 25-hydroxyvitamin D requirements to prevent nutritional rickets in Nigerian children on a low-calcium diet—a multivariable reanalysis. Am J Clin Nutr 2021 Mar 19.
[22] Miller ME, Higginbottom M, Smith DW. Short umbilical cord: its origin and relevance. Pediatrics 1981;67:618–21.
[23] Raum K, Grimal Q, Varga P, Barkmann R, Glüer CC, Laugier P. Ultrasound to assess bone quality. Curr Osteoporos Rep 2014 Jun 1;12(2):154–62.

[24] Wright D, Chan GM. Fetal bone strength and umbilical cord length. Perinatol 2009;29:603–5.
[25] Gursoy T, Yurdakok M, Hayran M, Korkmaz A, Yigit S, Tekinalp G. Bone speed of sound curves of twin and singleton neonates. J Pediatr Endocrinol Metabol 2008;21(11):1065–72.
[26] Park SH, Lee GM, Moon JE, Kim HM. Severe vitamin D deficiency in preterm infants: maternal and neonatal clinical features. Korean J Pediatr 2015;58:427–33.
[27] Sipponen P, Harkonen M. Hypochlorhydric stomach: a risk condition for calcium malabsorption and osteoporosis? Scand J Gastroenterol 2010;45:133–138.5.
[28] Malchodi L, Wagner K, Susi A, Gorman G, Hisle-Gorman E. Early acid suppression therapy exposure and fracture in young children. Pediatrics 2019 Jun 7:e20182625.
[29] Matsuda Y, Maeda Y, Ito M, Sakamoto H, Masaoka N, Takada M, et al. Effect of magnesium sulfate treatment on neonatal bone abnormalities. Gynecol Obstet Invest 1997;44(2):82–8. 10. Garcia et al. Rib fractures in children: A marker of severe trauma. J Trauma 30:695-88, 1990.
[30] Petersen S, Gotfredsen A, Knudsen FU. Total body bone mineral in light-for-gestational-age infants and appropriate-for-gestational-age infants. Acta Pædiatrica 1989 May;78(3):347–50.
[31] Holick MF, Hossein-Nezhad A, Tabatabaei F. Multiple fractures in infants who have Ehlers-Danlos/hypermobility syndrome and or vitamin D deficiency: a case series of 72 infants whose parents were accused of child abuse and neglect. Derm Endocrinol 2017 Jan 1;9(1):e1279768.
[32] Garcia VF, Gotschall CS, Eichelberger MR, Bowman LM. Rib fractures in children: a marker of severe trauma. J Trauma 1990 Jun 1;30(6):695–700.
[33] McMahon P, Grossman W, Gaffney M, Stanitski C. Soft-tissue injury as an indication of child abuse. JBJS 1995 Aug 1;77(8):1179–83.
[34] Ayoub DM, Hyman C, Cohen M, Miller M. A critical review of the classic metaphyseal lesion: traumatic or metabolic? Am J Roentgenol 2014 Jan;202(1):185–96.
[35] Miller M, Mirkin LD. Classical metaphyseal lesions thought to be pathognomonic of child abuse are often artifacts or indicative of metabolic bone disease. Med Hypotheses 2018 Jun 1;115:65–71.