Clinician's Corner

A 4-week-old infant with wheezing and abnormal movementsMarie-Pier Lirette MBChB^{1,✉}, Jennifer Harrington MD², Estelle B. Gauda MD³¹Pediatric Resident, The Hospital for Sick Children, Toronto, Ontario; ²Department of Endocrinology, The Hospital for Sick Children, Toronto, Ontario; ³Neonatal Intensive Care Unit, The Hospital for Sick Children, Toronto, Ontario**Correspondence:** Marie-Pier Lirette, The Hospital for Sick Children, 8 Charlotte Street, 555 University Avenue, Toronto, M5G 1X8, Canada. Telephone 416-802-5198, e-mail: marie-pier.lirette@sickkids.ca**PRESENTATION**

A 4-week old male infant born at 35 weeks of gestation was brought to a community hospital with abnormal breathing and eye deviation associated with limb stiffening. On arrival, oxygen saturation was 75% and there was significant work of breathing with bilateral wheeze, which improved with non-invasive ventilation and supplemental oxygen of 50%. Beta-2 agonists were not administered. He had peripheral hypertonia, clonus, and bilateral weak plantar grasps. He was afebrile with a normal blood glucose.

The infant was born during the winter period to a healthy G3P2 mother from Africa, currently living in a shelter. No resuscitation was required at birth, and the infant was discharged home after 24 hours. He was exclusively breastfed, received no medications or supplements, and was gaining weight and developing normally.

The infant was transferred to a tertiary neonatal intensive care unit where non-invasive ventilation and oxygen therapy were slowly weaned. He had a negative nasopharyngeal swab for

viruses; negative blood, urine, and cerebrospinal fluid cultures; and a normal electroencephalogram, although this did not capture any abnormal movements. The brain magnetic resonance imaging was non-contributory. The complete blood count and C-reactive protein were within normal limits and further blood-work is shown in Table 1.

Table 1. Further investigations

Investigation	Value	Normal range
Total calcium	1.18 mmol/L	2.08–2.64 mmol/L
Ionized calcium	0.72 mmol/L	1.22–1.37 mmol/L
Parathyroid hormone	111 ng/L	10–65 ng/L
25-Hydroxy vitamin D	6 nmol/L	50–250 nmol/L
Phosphate	3.18 mmol/L	1.56–2.67 mmol/L
Alkaline phosphatase	408 U/L	131–476 U/L
Creatinine	20 µmol/L	13–33 µmol/L
Magnesium	0.67 mmol/L	0.70–0.95 mmol/L

DISCUSSION

Symptomatic hypocalcemia of infancy is a medical emergency and can present with a range of symptoms including seizure-like activities, myoclonic jerks, jitteriness, and apnea, as summarized in Table 2. Wheezing due to low calcium is an unusual sign thought to be related to bronchospasm of the lower airways (1).

A basic work-up for neonatal hypocalcemia should include both total and ionized calcium as total calcium can be falsely low in the context of hypoalbuminemia and measurements of ionized calcium can be artificially low with alkalosis (such as with a respiratory alkalosis from prolonged crying) or incorrect collection of the sample. Phosphate, alkaline phosphatase, albumin, parathyroid hormone (PTH), creatinine, blood gas, magnesium as well as 25-hydroxyvitamin D, though not always readily available, measurements should also be done to help identify the underlying etiology.

The differential diagnosis of neonatal hypocalcemia includes vitamin D deficiency, maternal hyperparathyroidism, hypomagnesemia, and syndromes that are associated with hypoparathyroidism, such as 22q11 deletion. PTH level, usually available within a few hours, is particularly helpful as it can help differentiate between hypoparathyroidism and vitamin D deficiency.

A diagnosis of vitamin D deficiency was quickly and confidently made based on the routine bloodwork (low calcium and high PTH) as well the patient's many risk factors: prematurity, darker skin, born in winter months with decreased ultraviolet exposure, and exclusively breastfed with no vitamin D supplements. This diagnosis was later confirmed by a low 25-hydroxyvitamin D level

in both the infant and the mother. Vitamin D deficiency in pregnancy is another independent risk factor and this mother was at higher risk given her vulnerable social condition. Vitamin D deficiency typically presents in the newborn period with symptoms of hypocalcemia, as described above. Congenital rickets rarely presents this early and the infant, though being at high risk, did not have any features of congenital rickets such as enlarged fontanelles or craniotabes. Bony abnormalities, as per Table 2, do not present in this age group. Alkaline phosphatase is usually elevated in vitamin D deficiency, and phosphate level can be affected by gestational age, sex, and renal function.

Calcium infusion is recommended versus a bolus of calcium in order to prevent cardiac arrhythmia and extravasation injuries. Close follow-up measurements of total and ionized calcium should be conducted once started on an infusion and consultation with a paediatric endocrinologist is recommended. Once the calcium level normalized with a calcium infusion, the infant's wheezing, abnormal movements, and neurological examination resolved.

Supplemental vitamin D is relatively safe in newborns and pregnant women, and clinicians should promote its use. The Canadian Paediatric Society (CPS) recommends at least 400 IU of vitamin D per day for most newborns and 800 IU for those with risk factors. CPS also recommends at least 600 IU for pregnant women, given the association between vitamin D deficiency in the mother and neonatal hypocalcemia (2). Vitamin D deficiency in the newborn, though less common since public health initiatives such as fortification of dairy products, continues to be an important preventable disease in which

Table 2. Clinical features of hypocalcemia and vitamin D deficiency rickets

Age at presentation	Clinical features of hypocalcemia	Clinical features of vitamin D deficiency rickets
Infants	<ul style="list-style-type: none"> • Seizures • Abnormal movements • Jitteriness • Apnea/tachypnea; rare: wheeze (bronchospasm), stridor (laryngospasm), vomiting (pylorospasm) 	<ul style="list-style-type: none"> • Craniotabes (softening of the skull with delayed closure of fontanelles) • Frontal bossing • Large anterior fontanelles
Children	<ul style="list-style-type: none"> • Seizures • Tetany • Carpopedal spasm/muscle cramps • Paraesthesia/numbness • Perioral tingling • Prolonged QT interval • Myocardial dysfunction • Increased intracranial pressure/papilledema 	<ul style="list-style-type: none"> • Musculoskeletal: Genus Varus, bone pain, widened epiphysis, fractures, scoliosis • Delayed motor milestones • Muscle weakness • Rachitic rosary (enlargement of costochondral junctions) • Poor growth • Enamel hypoplasia/delayed dentition • Harrison's grooves (horizontal groove at the insertion of the diaphragm in the lower thorax)

paediatricians play a crucial role in advocating and recommending vitamin D supplementation.

CLINICAL PEARLS

1. The differential diagnosis for an infant presenting with abnormal movements is broad and initial investigations should include blood glucose, sodium, potassium, total and ionized calcium as well as magnesium.
2. Neonatal hypocalcemia can present with a range of symptoms including seizure-like activity, apnea, and more rarely bronchospasm. PTH level is crucial in helping the clinician differentiate between hypoparathyroidism and vitamin D deficiency, the most common cause.
3. Clinicians play an important role in preventing vitamin D deficiency by promoting vitamin D supplementation, especially in high-risk infants such as those born prematurely, with darker skin, exclusively breastfed with no supplementation and those in more vulnerable social situations.

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References

1. Abrunzo T. An infant fatality associated with inspiratory and expiratory wheezing: Another wheeze that wasn't asthma. *Pediatr Emerg Care* 1995;11(1):48-51.
2. Godel J. Vitamin D Supplementation: Recommendations for Canadian Mothers and Infants. Canadian Paediatric Society. October 2007. <<https://www.cps.ca/en/documents/position/vitamin-d>> (Accessed January 2017).