Dexamethasone-Induced Bradycardia in a SARS-CoV-2 Positive Neonate with Bilateral Congenital Dacryocystoceles

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Abstract

We present a case of a term neonate perinatally infected with SARS-CoV-2 who developed asymptomatic transient bradycardia due to IV dexamethasone during treatment for bilateral congenital dacryocystoceles. While cases of steroid-induced bradycardia are reported in older children and adults, the incidence in neonates is unknown, given the relative paucity of use in this population. In addition, it is unclear if this effect may be compounded or complicated by acute infections with SARS-CoV-2. Neonates treated with steroids, especially in the setting of infections with SARS-CoV-2, should be monitored with telemetry for the development of bradycardia.

Keywords: Steroid-induced bradycardia, dexamethasone-induced bradycardia, COVID-19, SARS-CoV-2

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Introduction

Bradycardia is an important finding in neonates due to the associated risk of increased mortality. While there are multiple associated etiologies, bradycardia has rarely been reported due to systemic corticosteroid use. Furthermore, bradycardia has been reported in individuals acutely infected with SARS-CoV-2. However, the concomitant occurrence and potential increased risk for developing bradycardia in neonates with known SARS-CoV-2 infections receiving systemic corticosteroids are unknown. We present a neonate with congestion due to nasolacrimal duct obstructions from bilateral congenital dacryocystoceles in the setting of a perinatally acquired infection with SARS-CoV-2 that developed asymptomatic bradycardia after receiving IV dexamethasone.

Case Presentation

The patient was a 5-day-old 3400g female born at 39 0/7 weeks gestation to a 38-year-old G1P0 mother who presented to our institution with a chief complaint of nasal congestion. The mother had an unremarkable prenatal course, and delivery was without complications. Prenatal labs were negative, including GBS. However, on routine screening prior to induction, she had a positive SARS-CoV-2 PCR – the mother remained asymptomatic before and after delivery. The infant also had a positive SARS-CoV-2 PCR on day of life 1. On day of life three, the parents reported an episode of self-resolving perioral cyanosis. On day of life 4, she developed significant congestion with swelling and a bluish appearance of bilateral nasolacrimal duct sacs and was taken to an outside hospital, at which point repeat testing continued to be positive for SARS-CoV-2. She was recommended to perform nasolacrimal duct massages with warm compresses and sent home, but due to worsening congestion with decreased bottle feeding presented to our ED the following day.

On arrival to our ED, she was noted to have significant swelling near the medial canthus bilaterally with palpable firm cystic masses near the superior aspect of the nasolacrimal duct (Figure One) and was observed to have a drop in oxygen saturation to 85% during feeding. She was admitted to the Pediatric Hospitalist service, and Pediatric ENT and Pediatric Ophthalmology were consulted. Pediatric ENT performed a bedside flexible fiberoptic evaluation and noted bilateral dacryocystoceles with nasal obstruction. She was started on oxymetazoline, one drop per nostril every 12 hours, with mild improvement. On day of life 6, she was brought to the operating room by Pediatric Ophthalmology for lacrimal duct probing and received interoperative ophthalmic antibiotics as well as preoperative IV Dexamethasone 2mg (0.58mg/kg). She tolerated the procedure well and was noted to have improved nasal congestion immediately postoperatively. However, the following day, she had a recurrence of nasal congestion complicated by expiratory stridor and increased use of accessory muscles, so she was given IV Dexamethasone 2 mg approximately 18 hours after her preceding dose and a second flexible fiberoptic evaluation performed by ENT was concerning for near complete bilateral nasal obstruction from postoperative edema. She was given nasal saline drops and oxymetazoline to improve her congestion. However, approximately 3.5 hours after administration of systemic steroids, she was noted to develop persistent new-onset bradycardia while awake in the 70s with a nadir of 69 without associated desaturations.

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Given the persistent bradycardia, she was transferred to the pediatric intensive care unit at which point a full work-up was performed, including complete blood count (CBC), blood culture, electrocardiogram (EKG), venous blood gas (VBG), comprehensive metabolic panel (CMP), elevated sedimentation rate (ESR), ferritin, d-dimer, pro-brain natriuretic peptide (pro-BNP), urinalysis with urine culture, head ultrasound, and chest

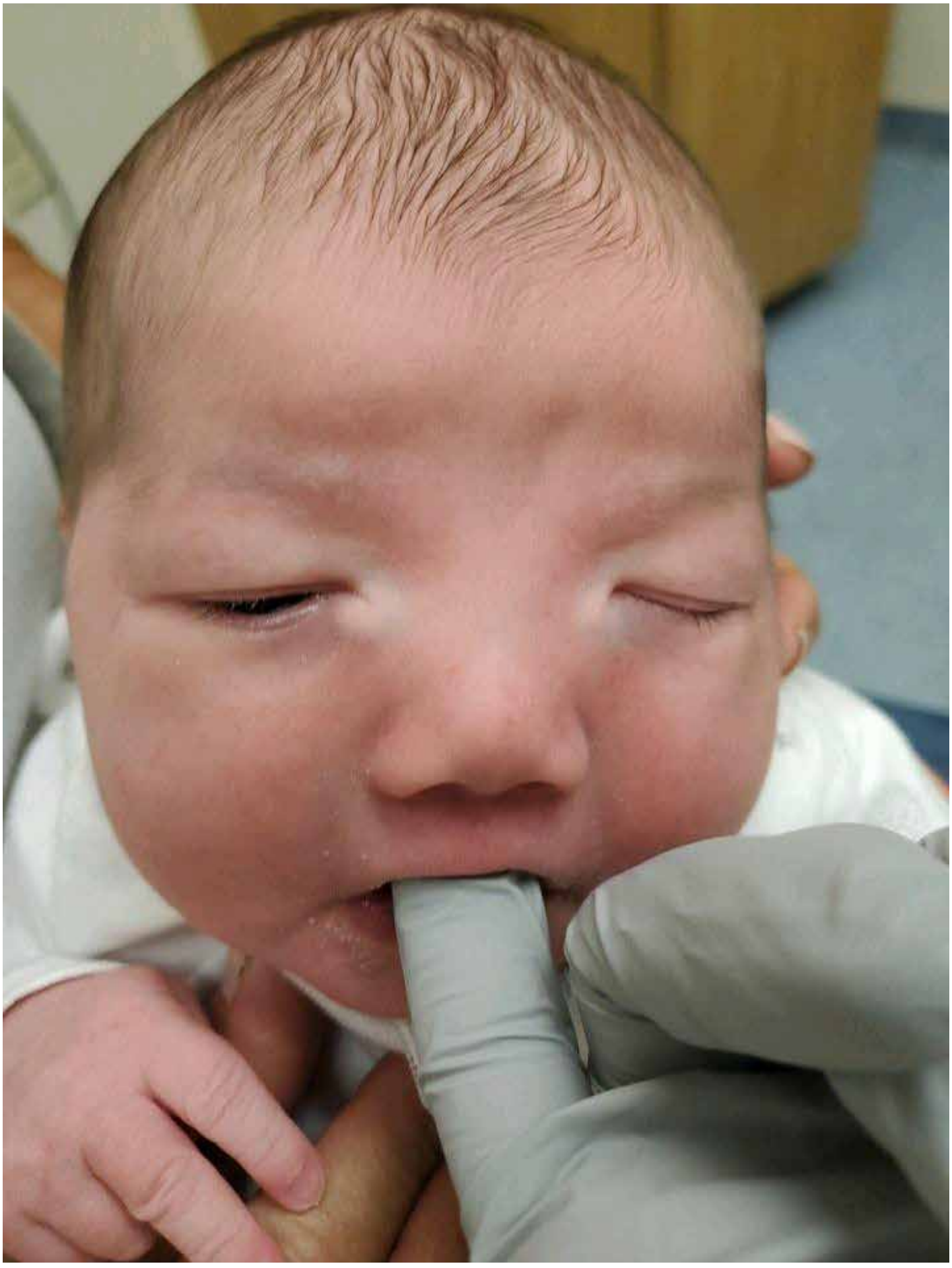

Figure 1: (Left) Preoperative bilateral dacryocystoceles; (above) One day postoperatively from probing of bilateral dacryocystoceles

and abdomen x-rays. Labs were only significant for ferritin of 872 and pro-BNP of 5429. The electrocardiogram showed sinus bradycardia. On day of life 8, pro-BNP had decreased without intervention to 3159, and an echocardiogram was performed, showing a small patent foramen ovale, normal LV function, normal proximal coronary arteries, and no pericardial effusion. Of note, her newborn state screens later returned as normal. Her bradycardia resolved without intervention within 12 hours from the onset, and she was transferred back to the Pediatric Hospitalist service for observation and then discharged at nine days of life in good condition.

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Discussion

We present the case of a term neonate found positive for SARS-CoV-2 at birth with nasolacrimal duct obstruction due to bilateral congenital dacryocystoceles that developed acute asymptomatic bradycardia suspected secondary to IV dexamethasone administration. This bradycardia was self-limited, occurring ~4 hours after systemic corticosteroid use and resolved within 12 hours from onset. Although referenced in general pediatric and adult literature, reports of steroid-associated bradycardia in neonates are rare, especially given the less common usage of systemic steroids in this population compared to older patients. Furthermore, its occurrence in SARS-CoV-2-positive neonates is unknown.

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Bradycardia is a not uncommon yet concerning finding in neonates that may be due to multiple etiologies and warrants a thorough evaluation, given the high associated mortality. While more common in premature infants, the differential diagnosis in term newborns includes congenital heart block due to maternal systemic lupus erythematosus, sepsis, hypoxia, hypothermia, congenital hypothyroidism, congenital heart disease or congenital arrhythmias (e.g., Congenital Long QT Syndrome), central nervous system disturbances and electrolyte abnormalities (e.g., Hypoglycemia). A thorough evaluation of the above was performed in our infant and found negative, at which point the suspected causal agent was thought to be IV dexamethasone.

Corticosteroids are known to have many acute and chronic adverse effects, most commonly: hypertension, electrolyte abnormalities (hyperglycemia, hypokalemia), behavioral changes, immune suppression with subsequently increased rates of infections, and sudden death (1,2). In the neonatal population, there are additional risks of spontaneous gastrointestinal perforation and the development of hypertrophic cardiomyopathy (3,4). While arrhythmias have been reported in the literature, a majority are associated with tachyarrhythmias as opposed to bradycardia. First reported in 1986, corticosteroid-induced bradycardia is a rare albeit not entirely unknown side effect seen in children and adults (1,5-11). Multiple case reports show this effect may occur after IV or PO administration with various agents, most notably in treating rheumatologic and oncologic conditions – particularly methylprednisolone and dexamethasone. The effect is mainly dose-dependent and may be questionably related to the speed of administration (e.g., IV bolus vs. drip). While the development of bradycardia has sometimes required pressor support in adults, it is generally asymptomatic in children. One case reported the development of asymptomatic bradycardia in a child treated with protocol-defined doses of IV methylprednisolone for multisystem inflammatory syndrome in children (a.k.a. MIS-c) (12).

In neonates, corticosteroids are sometimes used for bronchopulmonary dysplasia and hyaline membrane disease and to facilitate extubation (e.g., DART Protocol) (3,13). However, this protocol calls for a lower dose of dexamethasone of a cumulative 0.89mg/kg – our infant received a total of 1.15mg/kg within 24 hours. Limited case reports in the 1980s reported the development of persistent bradycardia in premature infants treated with dexamethasone at doses similar to that received by our14-16; however, these cases predate the era of SARS-CoV-2.

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The exact mechanism for corticosteroid-induced bradycardia is unknown; however, animal studies suggest direct effects on myocytes via alterations in cardiovascular sensitivity to catecholamines, along with acute electrolyte shifts accompanied by alterations in sodium and water physiology. These changes are proposed to lead to an expansion of plasma volume with relative hypertension and activation of a baroreceptor response (1,2,5,6,8). However, these electrolyte changes are challenging to detect and generally tolerated by most infants without other underlying diseases. Furthermore, tracking of consistent elevation of blood pressure with simultaneous decreases in heart rate is difficult to obtain. In our patient, electrolytes, EKG, and echocardiogram were normal and blood pressure, while intermittently elevated, was difficult to correlate directly with the drop in heart rate.

Particularly of interest in our patient was an acute infection

with SARS-CoV-2. While her congestion was suspected mainly secondary to duct obstruction, it is difficult to determine if her symptoms or postoperative course were worsened by concomitant infection. Several studies have reported the presence of arrhythmias among individuals with SARS-CoV-2. While most reported are tachyarrhythmias, specifically sinus tachycardia or supraventricular tachycardias, relative bradycardia has been reported in adult literature to account for up to 12% of cardiac dysrhythmias, often as a marker of cardiovascular collapse (17-19).

Furthermore, increasing reports have noted an association between perinatal transmission of SARS-CoV-2 infection and bradycardia. In a study of 130 neonates in Jordan, sinus bradycardia was reported to occur in 18.8% of SARS-CoV-2 positive neonates as opposed to 1.8% of SARS-CoV-2 negative neonates; however, the time of exact occurrence of bradycardia was not reported. Bradycardia associated with acute SARS-CoV-2 infection has been thought to be multifactorial due to severe hypoxia, inflammatory damage of cardiac pacemaker cells, and exaggerated response to medications (20,21).

While it is difficult to conclude that an acute infection compounded our infant's response to IV corticosteroids with SARS-CoV-2, further studies should be undertaken to evaluate this risk. Presumably, viral damage of cardiomyocytes may predispose or exaggerate newborns' response to corticosteroid-associated bradycardia development.

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Conclusion

We present the case of a newborn with significant nasal congestion due to bilateral congenital dacryocystoceles and acute infection with SARS-CoV-2 that developed asymptomatic self-limited bradycardia after the administration of IV dexamethasone. Bradycardia is suspected to be from corticosteroid use due to alterations in cardiovascular sensitivity, baroreceptor response, and electrolyte shifts, as well as in acute infections with SARS-CoV-2 due to cardiomyocyte damage and inflammation due to viral infiltration. The concomitant use of steroids in active SARS-CoV-2 infections may compound resultant bradycardia, and thus neonates should be monitored carefully with telemetry in these situations.

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