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Dates: Received: 07 April, 2017; Accepted: 22 May, 2017; Published: 24 May, 2017

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Keywords: Stridor; Hypocalcemia; Vitamin D deficiency; Laryngeal narrowing; Bronchogenic cyst; Laryngomalacia

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Review Article

Hypocalcemic Rachitic Stridor: A Neglected Warning Sign in Infants

Abstract

Although stridor is a common respiratory symptom associated with upper respiratory diseases, yet its relation with hypocalcemia is not widely appreciated. The mechanism of hypocalcemia in causing stridor might be a collapsing of larynx most likely caused by decalcification due to hypocalcemia. Vitamin D deficiency causes a reduction in serum calcium, which stimulates the production of extra PTH to mobilize and maintain calcium from bone and cartilage for more vital cells of the body, brain, heart and blood. Stridor might appear with upper respiratory tract infection, accordingly the role of hypocalcemia as a cause of stridor might not be recognized. Infants are born with poor vitamin D in places with high prevalence of vitamin D deficiency due to environmental, social, customs and housing factors. Due to maternal vitamin D deficiency, breast milk is low in vitamin D which leads to poor absorption of calcium. Stridor caused by hypocalcemia should be considered as a warning sign to prevent more serious complications as cardiomyopathy, myelofibrosis, and convulsions. In communities with high prevalence of vitamin D deficiency checking for hypocalcemia should be part of the work up, when stridor is the presenting symptom in infants. The mechanism by which hypocalcemia causes stridor might be laryngomalacia.

Introduction

Stridor is a noisy breathing in infants or older children, usually frightening to parents. John Apley [1] said while answering a question what is strider:

“For an answer, I consulted not only doctors and dictionaries, but also parents and poets. The word strider is derived from Latin strider, to make gratingly shrill or harsh noise. It needs to be harsh and vibrating, though it should be sustained or repeated, mothers tell me that their child coos like a dove, or purrs like a cat or grunts like a piggy or makes a wheezing, grunting, or sieving noise. Thackeray writing of the healthy baby who would crow with delight is my exemplars for my theme is that in the diagnosis of strider we should consider more than the noise. The high-pitched crowing sound of laryngospasm due to tetany may be diagnosed as laryngeal stridor. The mistake is most likely in tetany of the newborn, but it may be made also in older children with increased neuromuscular instability, provoked by a state of alkalosis, whether due to celiac disease, rickets, hypoparathyroidism, renal failure or hyperventilation.”

Stridor is an abnormal high-pitched sound produced by turbulent airflow through a partially obstructed airway at the level of the supraglottis, glottis, subglottic, and/or trachea. The tonal characteristics of the sound are extremely variable (IE, harsh, musical, or breathy); however, combined with the pace, volume, duration, rate of onset, and associated symptoms, the tonal characteristics may provide additional diagnostic clues.

In all cases, it should be differentiated from the startle, which is a lower-pitched, snoring-type sound generated at the level of the nasopharynx, oropharynx, and, occasionally, supraglottic.

Stridor is a symptom, not a diagnosis or disease, and the underlying cause must be determined. Stridor may be inspiratory, expiratory, or biphasic depending on its timing in the respiratory cycle. Inspiratory stridor suggests a laryngeal obstruction, while expiratory stridor implies tracheobronchial obstruction. Biphasic stridor suggests a subglottic or glottis anomaly. In addition to a complete history and physical, as well as other possible additional studies, most cases require flexible and/or rigid endoscopy to evaluate the etiology of stridor adequately.

As we see many cases of nutritional rickets, in which hypocalcemic convulsions is the commonest presentation in the first year of life [2] and as it might be associated with other rare complications as cardiomyopathy [3] and myelofibrosis [4] and as well as iron deficiency anemia [5] and as stridor is a serious complication jeopardizing respiration and as hypocalcemia due to vitamin D deficiency is not uncommon, it is reviewed in this communication.

Review and Results

PubMed was reviewed for stridor and hypocalcemia. It revealed 22 publications which were reviewed, 15 out of these publications were discussing the association between stridor

and hypocalcemia of which two were in elderly people and the rest were mostly case reports in infants as described in table 1. Most of them were male aged between a few days to 16 months. Stridor was the presenting feature in all cases with or without convulsions, but all were having hypocalcemia. These cases were reported from a wide range of countries, but the cases in temperate countries were among immigrants from Africa, Asia or Hispanics. The ages in the majority were under one year and all were breastfed. Two were elders one with previous thyroidectomy leading to chronic hypocalcemia and stridor.

General causes of stridor

Noisy breathing to be termed stridor was observed in laryngo-tracheo-bronchitis, foreign body, laryngomalacia and many other congenital and acquired causes. The cause which is discussed in this communication is not given in Medscape, may be because it is rare.

Hypocalcemia as a cause of stridor in medical literature is shown in the table. Four reports from each of USA, and UK. In addition, two from each of Spain, and India and one from Taiwan. These infants were six boys and one girl and the rest were introduced as infants without giving their gender. All were dark skinned living in temperate countries. The ages of the infants varied from eight days to 17 months at presentation and their mean age was 7.5 months. All presented with stridor and respiratory distress and all were found to have hypocalcemia with high alkaline phosphatase and PTH. There was clinical evidence of rickets in older infants.

Pathophysiology of stridor in hypocalcemia

The narrowing of the upper part of the respiratory tract causes a turbulence of air flow manifested as stridor, usually observed in upper respiratory tract infection or foreign body inhalation [5].

Table 1: Causes of stridor in general.

Acute stridor	Chronic stridor
Laryngo-tracheo-bronchitis 1-3y	Laryngomalacia
Aspiration of foreign body	subglottic stenosis
Bacterial tracheitis	Acquired stenosis (post intubation)
Retropharyngeal abscess	Vocal cord dysfunction paralysis
Peritonsillar abscess	Vocal cord cyst
Spasmodic croup, 1-3y	Laryngeal subglottic hemangioma
Allergic airway edema 1-7y	Laryngeal web (congenital)
	Laryngeal dyskinesia, exercise-induced
Epiglottitis 3-7	Laryngeal cysts
	Laryngeal papillomas
Hypocalcemia	Tracheomalacia
	Tracheal stenosis
Bronchogenic cyst	Choanal atresia (bilateral)
	Laryngeal TB
	Redundant aryepiglottic fold (Peron1988) [16]
	suprasternal bronchogenic cyst [17]
	Congenital Saccular Cyst of the Larynx: A

Modified from Medscape.

As we are seeing rising cases of rickets presenting with hypocalcemia and occasionally with stridor that might be misdiagnosed as viral croup, I am reviewing the relation between stridor and hypocalcemia. Although stridor is a common respiratory symptom associated with upper respiratory diseases, yet its relation with hypocalcemia is not widely appreciated. The mechanism of hypocalcemia in causing stridor is most likely a sort of laryngeal collapse due to loss of its rigidity caused by hypocalcemia which is obvious in the early phase of rickets. In infancy rickets starts with hypocalcemia due to lack of vitamin D. In this phase the bony features of rickets are not obvious. It is when the parathyroid glands are stimulated by the hypocalcemia that an excess of parathormone mobilizes the calcium from the bones and cartilage leading to decalcified bones and softening of cartilage, which in this phase present as stridor due to collapse of the larynx. Narrowing associated with edema, foreign body, or pressure from outside in addition to softening and narrowing of the larynx due to hypocalcemia is what is causing stridor, also aggravated by upper respiratory infections, that is why the role of hypocalcemia in stridor is not well appreciated. Hypocalcemia stimulates parathyroid glands to secrete extra hormone needed to mobilize calcium from bone and cartilage with a more vital objective to maintain enough calcium for brain, heart and blood. In places with prevalence of vitamin D deficiency, breast milk is low in vitamin D due to maternal vitamin D deficiency. Stridor caused by hypocalcemia should be recognized early and treated promptly taken as a warning sign of occult rickets that might herald serious complications as convulsions [2], cardiomyopathy [3] and myelofibrosis [4]. The development of stridor is not as common as the other features of rickets. Due to the hyperparathyroidism playing a major role in correcting the blood level of calcium.

Bronchogenic cyst

Bronchogenic cysts as a cause of stridor has been reported from different parts of the world. All of them presented with noisy breathing since birth with variable degrees. Ironically, a case was diagnosed following a peanut aspiration which was taken as the cause of stridor which persisted after surgical removal to diagnose the primary cause of stridor. The details are shown in table 2. All improved with the disappearance of stridor post operatively. This is a rare curable cause of stridor. Although hypocalcemia is not a common cause, it is essential to think of it together with other common causes of stridor, specially these mostly congenital cases presents as early as the first day in life, in contrast to hypocalcemic might be observed after the first week of life [6].

Other causes of stridor

There are many causes of stridor as shown in table 3 which might be acute or chronic with some of them being very serious with high mortality and needs urgent recognition and prompt management. Stridor in infants can be life threatening and pediatricians and all practitioners and all medical assistants need to be aware of managing this problem. Hypocalcemia as a cause of stridor need to be thought of, as it dramatically

Table 2: Hypocalcemic Stridor.

Reference year nno[No]	County	Age mon	Sex	Pre-Sent	CP	XR	Fed	Ca Mg/ml	Ph M/ml	Alk iu	PTH Pg ml	25OHD mol	Management	oooutcom
Venkatesh 2012 [8]	Inda	4	m	Coughs	ST conv		Bo	7.5	L	H		4.7	Ca vit DR	REc
Chehad 2011 [9]	Swis	16	m	CRA	CRA	+r	Bf	1.1	L	1300	325	5.7	R, CA D	Rec
Walter 2010 [10]	Span	6 7	m m	Conv ST	Rickets Ric	AR AR	Bf bf	6 5.6	3.8 6.4	713 440	14.1 18.4	8.9 9.6	viD Ca vitCa	Rec Rec
Naeer 2007 [11]	UK	8d	m	ST Days	22q11 del Sin, stridor		BF	L	L	H	H	L	VD CA	
Murphy 2006 [12]	USA	inf		Stridortetany	Renal dysplasia		B F	L	L	H	H	L	Usual	Rec
Duplechin 1999 [13]	USA	17		ST	Rickets		BF	L	L	H	H	L	Ca vitD	Rec
Halterman 1998 [14]	USA	inf		ST	Rickets		BF	L	L	H	H	L	Vit D, CA	Rec
Abrunzo 1995 [15]	USA	inf		ST	RD		BF	L	L	H	H		Ca vitD	died
Patier 1995 [16]	Span	inf		ST				L	L	H	H	L		Rec
Sherief 1991 [7]	UK	11m	m	ST Crying	BH, BL WR	No	BF	1.23	L	2744	340	4.7	Vitd Ca	REC
Hsu 1995 [17]	Tain	inf	f	P De gorge	Stridor	n	BF	L	L	H	H	L	vitD ,Ca	Rec
Train 1995 [18]	UK	5 7		ST ST	RD RD		BF	1.1 0.9	L L	411 1406	118 195	<2.5	Vitd &Ca	Rec Rec
Strivastava 2008 [19]	UK	ld		ST	Chronic	n		L	L	H	L	L	VITD 7CA	Rec
Buyukcam 2010 [20]		Eler		ST	Postthyroi	n	ectom	L	L	H	H	L	Ca vitD	Rec
Gupta 1989 [6]	India	7m		ST	RD		Bf	L	L	H	H	L	Ca VitD	Rec
Abraham 2013 [21]	UK	11y		ST	Raphael			L	L	H	H	L	Dialysis	ransplanted

RD respiratory distress BH: bossing Head, BL: bow legs, WR: wide wrists ST: stridor, Rec: recovered, Conv: convulsions, Dys: dysmorphic AR: radiologically active rickets CRA: cardio-respiratory arrest. A 4-22Q11 syndrome with: congenital heart defects, facial dysmorphism, palatal defects, feeding problems, immune deficiency and hypocalcaemia... 10- partial DiGeorge anomaly associated with a distal chromosome 10p deletion. 22q11 deletion: dysmorphic features of the face, with, mainly congenital heart defects, palatal defects, feeding problems, immune deficiency and hypocalcaemia.

Table 3: Reported cases of Stridor due to Bronchogenic Cyst in Infants.

Reference [N]	Country	Age, gn	Presentation	Diagnosis, management	P
Richard 1988 [21]	France	Newborn	Respiratory distress	Bronchogenic cyst compressing the trachea surgical	G
Herdry 1988 [22]	UK	Child	Persistent stridor.	Ultrasonic diagnosis of a bronchogenic cyst	G
Lazar 1991 [23]	USA	Newborn	With stridor	Severe respiratory distress caused by a mediastinal bronchogenic cyst	G
Bohle 1999 [24]	Germany	5m infant	Acute respiratory insufficiency	Tracheogenic cyst	G
Stewart 2002 [25]	USA	Infant	Wheeze, stridor, and retractions	Midtracheal bronchogenic cyst.	G
Mampilly 2005 [26]	India	Infant	Refractory wheezing	Bronchogenic cyst – cause of refractory wheezing in infancy	G
Jackson 2006 [27]	Sweden	1.5-yr - M	Recurrent wheezing, severe episodes after a peanut aspiration.	Wheezing persisted, evaluation revealed a bronchogenic cyst	G
Reilly 2006 [28]	USA	Infant:	Stridor	Bronchogenic cyst	G
Artz 2006 [29]	USA	Infant	Stridor	Bronchogenic cyst	G
Lai 2006 [30]	Can	Infant:	Biphasic stridor in	An unusual case suprasternal bronchogenic	G
Zedan 2009 [31]	Egypt	4m F	Respiratory distress with stridor. A history of slowly progressive noisy breathing	Evidence of bilateral obstructive emphysema. Fiber-optic bronchoscopy: post. mediastinal compression, bronchogenic cyst.	G
-oswamy 2011 [32]	UK	6m- M	Right-sided, level IV neck lump 3m history of cough inspiratory stridor.	Mediastinal lesion was excised via an external approach. The histological diagnosis was a bronchogenic cyst	G
Busino 2011 [33]	USA	Neonate	Expiratory stridor		G

G: All recovered after surgery F: female M: male m: month.

responds to calcium and vitamin D therapy in adequate doses. As we are concentrating on hypocalcemic stridor [7], in this communication other causes were not discussed in details.

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