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 stridor:

“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 gratefully 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, laryngiomalacia 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 mostly case reports in infants as described in table 1. All of them presented with stridor and respiratory distress and all were found to have hypocalcemia. These cases varied from eight days to 17 months at presentation and 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].

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.

**Table 1: Causes of stridor in general.**

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

Modified from Medscape.
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.

References

1. Apley J [1965] Stridor in Children. Proc R Soc Med 58: 271–272. Link: https://goo.gl/htwVhi

2. Elidrissy ATH Sandokji A, Hawsawi ZM, Faleh Al-Magamsi MS [2012] Nutritional rickets in Almadinah al Munawarah: presentation and associated factors. J Taibah Uni MED SCI 7: 35-40. Link: https://goo.gl/cvCXXr

3. Elidrissy AT, Munawarah M, Alharbi KM (2013) Hypocalcemic rachitic Cardiomyopathy in infant's. J Saudi Heart Assoc 25: 25-33. Link: https://goo.gl/fh5aN0

Table 2: Hypocalcemic Stridor.

| Reference year | County | Age mon | Sex | Pre-Sent | CP | XR | Fed | Ca Mg/ml | Ph M/ml | Alk iu | PTH Pg ml | 25OHD mol | Management | ooooutcom |
|----------------|--------|---------|-----|----------|----|----|-----|----------|---------|--------|---------|-----------|-----------|------------|----------|
| Venkatish 2012 [8] | Inda 4 | m | Coughs | ST conv | Bo | 7.5 | L | H | 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 | Conv | ST | Rickets | Ric | AR | Bf | 6 | 5.6 | 3.8 | 6.4 | 713 | 440 | 14.1 | 18.4 | 8.9 | 9.6 | vitD Ca vitCa | Rec | Rec |
| Nae 2007 [11] | UK 8d | m | ST | Days | 22q11del Sin, stridor | BF | L | L | H | H | L | VD CA |
| Murphy 2006 [12] | USA | inf | Stridor | tetany | Rickets | B F | L | L | H | L | Usual | Rec |
| Duplechin 1999 [13] | USA | 17 | ST | Rickets | BF | L | L | H | L | V | Ca vitD | Rec |
| Halterman 1998 [14] | USA | inf | ST | Rickets | BF | L | L | H | L | Vit D, CA | Rec |
| Abrunzo 1995 [15] | USA | inf | ST | RD | BF | L | L | H | H | Ca vitD | died |
| Pater 1996 [16] | Span | inf | ST | BF | L | L | H | H | L | VD CA |
| Shereif 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] | UK | inf | 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 | 411 | 1406 | 118 | 195 | <2.5 | VitD &Ca | Rec | Rec |
| Strivastava 2008 [19] | UK | Id | ST | Chronic | n | L | L | H | L | L | VITD 7CA | Rec |
| Buyukcam 2010 [20] | Eler | ST | Postthyroi | 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 |

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 |
| Bohlé 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. Fiberoptic 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 P: female M: male m: month.
4. Eldrissy ATH, Zolaly MA, Hawsawi ZM [2012] Anemia in infants with vitamin D Deficiency Rickets: a single center experience and Literature Review. Journal of Applied Jo Hematology 3: 39-43. Link: https://goo.gl/M8pv2i
5. Eldrissy ATH, Zolaly MA, Hawsawi ZM [2012] Anemia in infants with vitamin D Deficiency Rickets: a single center experience and Literature Review. Journal of Applied Jo Hematology 3: 39-43. Link: https://goo.gl/M8pv2i
6. Gupta MM [1989] Medical emergencies associated with disorders of calcium homeostasis. Assoc J Physicians India 37: 629-631. Link: https://goo.gl/nNDz2N
7. Sharief N, Matthew DJ, Dillon MJ [1991] Hypocalcaemic stridor in children. How often is it missed? Clin Pediatr [Phil]a 30: 51-52. Link: https://goo.gl/3V77lle
8. Venkatesh C, Chhavi N, Gunasekaran D, Soundararajan P [2012] Acute stridor and wheeze as an initial manifestation of hypocalcemia in an infant. Indian J Endocrinol Metab 16: 320-321. Link: https://goo.gl/1POJK
9. Chehade H, Girardin E, Rosato L, Cachat F, Cotting J, et al. [2011] Acute life-threatening presentation of vitamin D deficiency rickets. J Clin Endocrinol Metab 96: 2681-2683. Link: https://goo.gl/fJeRMi
10. Walter C, Muñoz-Santanach D, Marín Del Barrio S, Corrales Magín E, Pou Fernández J [2010] Symptomatic hypocalcemia due to nutritional rickets. A presentation of two cases. An Pediatr [Barc] 72: 343-346. Link: https://goo.gl/xgbVW
11. Naeem KB, Ahmed M [2007] Stridor in a neonate—is it just a floppy larynx. J Pak Med Assoc 57: 322-323. Link: https://goo.gl/NYZf9c
12. Murphy G, Bartle S [2006] Hypocalcemic laryngospasm and tetany in a child with renal dysplasia. Pediatr Emerg Care 22: 507-509. Link: https://goo.gl/CPN6uJ
13. Duplechin RY, Nadkani M, Schwartz RP [1999] Hypocalcemic tetany in a toddler with undiagnosed rickets. Ann Emerg Med 34: 399-402. Link: https://goo.gl/DxHnmI
14. Halterman JS, Smith SA [1998] Hypocalcemia and stridor: an unusual presentation of vitamin D-deficient rickets. J Emerg Med 16: 41-43. Link: https://goo.gl/S3i2WZ
15. Abrunzo TJ [1995] An infant fatality associated with inspiratory and expiratory wheezing: another wheeze that was not asthma. Pediatr Emerg Care 11: 48-51. Link: https://goo.gl/LcMKQS
16. Patier JL, Campos L, Rivas FJ, Yañez E, Arrazola J [1995] Fever, generalized rigidity and stridor. Rev Clin Esp 195: 124-125. Link: https://goo.gl/Q2NTG0
17. Hsu HL, Siao PH, Hou JW, Tsai WY, Wang TR [1997] Partial DiGeorge anomaly associated with 10 p deletion. J Formos Med Assoc. 96: 996-999. Link: https://goo.gl/Hfdqla
18. Train JJ, Yates RW, Sury MR [1995] Hypocalcaemic stridor and infantile nutritional rickets. BMJ 7: 48-49. Link: https://goo.gl/ZkZzVP
19. Srivastava A, Ravindran V [2008] Stridor secondary to hypocalcemia in the elderly: an unusual presentation. Eur J Intern Med 19: 219-220. Link: https://goo.gl/VOqH43
20. Büyükkam F, Sönmez FT, Sahinli H [2010] A Delayed diagnosis: stridor secondary to hypocalpemia. Int J Emerg Med 3: 461-462. Link: https://goo.gl/uj0GW
21. Abraham D, Karuvattil R, Fitzpatrick M [2013] Stridor in an 11-year-old child. BMJ Case Rep. 2013 Dec 10;2013 pii: bcr2013201025. doi: 10.1136/bcr-2013-201025.
22. Richard O, Teyssier G, Rayet I, Chavrier Y, Girerd J [1988] Bronchogenic cysts compressing the trachea, an unusual cause of neonatal respiratory distress. Pediatr 43: 521-523. Link: https://goo.gl/ewfcF
23. Hendry PJ, Hendry GM [1988] Ultrasonic diagnosis of a bronchogenic cyst in a child with persistent stridor. Pediatr Radiol 18: 338. Link: https://goo.gl/FCwwH
24. Lazar RH, Younis RT, Bassila MN [1991] Bronchogenic cysts: a cause of stridor in the neonate. Am J Otolaryngology 12: 117-121. Link: https://goo.gl/GVlYsR
25. Böhle AS, Dohrmann P, Mengel W, Schröder H [1999] Acute respiratory insufficiency in an infant caused by a tracheogenic cyst. Thorac Cardiovasc Surg 47: 124-125. Link: https://goo.gl/Qo6ag
26. Stewart B, Cochran A, Iglesia K, Speights VO, Ruff T [2002] Unusual case of stridor and wheeze in an infant: tracheal bronchomalacic cyst. Pediatr Pulmonol 34: 320-323. Link: https://goo.gl/XRDMd0
27. Mampilly T, Kurian, R, Shenai A [2005] Bronchogenic cyst – cause of refractory wheezing in infancy. Indian J Pediatr 72: 363-364. Link: https://goo.gl/dyevGL
28. Jackson A, Simpson J, Coutts J [2006] An unusual cause of respiratory distress at birth. Diagnosis: bronchogenic cyst occluding the trachea. Acta Paediatr. 95: 1144-1147. Link: https://goo.gl/epFPe
29. Reilly J, Mattei P [2006] Stridor in an infant: commentary. Diagnosis: bronchogenic cyst. Clin Pediatr [Phil]a 45: 578-581. Link: https://goo.gl/kyQgXY
30. Arzt GJ [2006] Stridor in an infant. Clin Pediatr [Phil]a 45: 578.
31. Lai P, Nguyen LH, Kim PC, Campisi P [2006] Unusual case of biphasic stridor in an infant: suprasternal bronchogenic cyst. J Pediatr 149: 424. Link: https://goo.gl/QK0dWn
32. Zedan M, Elga mal MA, Zalata K, Nasef N, Fouda A [2009] Progressive stridor: another wheeze that was not asthma. Pediatr Emerg Care 25: 317-320. Link: https://goo.gl/nyE3L
33. Goswamy J, de Kruijf S, Humphrey G, Rothera MP, Bruce IA [2011] Bronchogenic cysts as a cause of infantile stridor: case report and literature review. J Laryngol Otol 125:1094-1097. Link: https://goo.gl/IWwEma
34. Busino RS, Quareshi HA, Cohen IT [2011] Stridor secondary to a bronchogenic cyst in a neonate. Ear Nose Throat J 90: EB-10. Link: https://goo.gl/RPuR3Q

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