Growth Hormone Unmasked Laryngomalacia and Worsened Obstructive Sleep Apnea in Infants with Prader-Willi Syndrome

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Background

- Prader-Willi Syndrome (PWS) is a genetic syndrome due to loss of expression from genes within the PWS imprinted region at chromosome 15q11.2-13
- Characteristics include hypothalamic-pituitary dysregulation, abnormal respiratory drive, and hyperphagia
- Growth hormone (GH), often started in infancy, improves tone, body composition, and height
- Mortality in children with PWS include those due to respiratory illness (61% incidence), choking (5% incidence), and sudden unexplained death (17 % incidence)[1]
- Concerns about sudden death in children with PWS started on growth hormone is hypothesized secondary to worsening obstructive sleep apnea (OSA) from adenotonsillar hypertrophy
- This has resulted in guidelines for polysomnography (PSG) evaluation before and after starting GH

Methods

- We report two cases of worsened OSA in infants with PWS after GH due to unmasked laryngomalacia

Case 1

- Female with PWS due to imprinting center epimutation.

Table 1. Timeline of Events – Case 1			
Age	**Polysomnography Results or Intervention**		
	AHI	**oAHI**	**nO2 (%)**
2 mo	15	12	94
Intervention: Start GH 0.5 mg/m^2/d at 2 mo			
4 mo	31	29	81
Intervention: Hold GH. FFL at 4 mo shows laryngomalacia (Image 1A)			
Intervention: Supraglottoplasty at 5 mo (Image 1B)			
6 mo	6	1.8	90
Intervention: Restart GH at 7 mo			
8 mo	6	4	88

A) B)

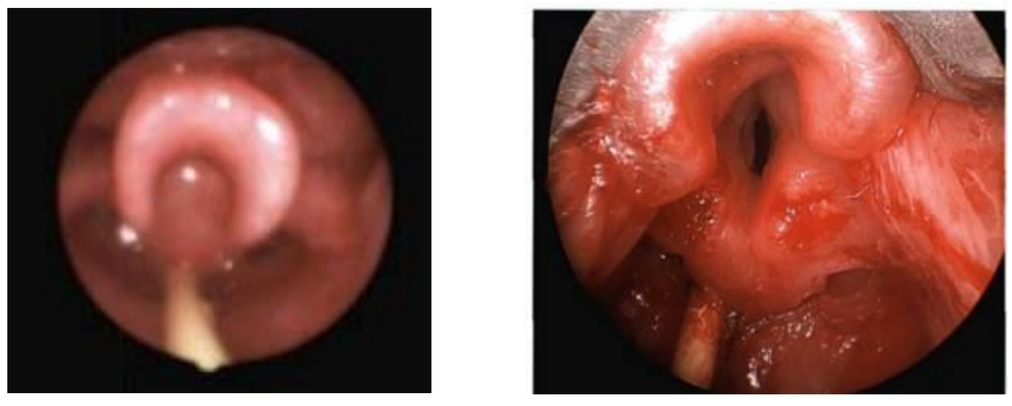

Image 1. Pre-Operative and Post-Operative Images for Case 1

A) Pre-operative image by FFL showing supra-arytenoid tissue prolapse indicative of laryngomalacia. B) Post-operative image by rigid endoscopy showing more patent airway after supraglottoplasty.

Case 2

- Female with PWS due to deletion.

Table 2. Timeline of Events – Case 2			
Age	**Polysomnography Results or Intervention**		
	AHI	**oAHI**	**nO2 (%)**
5 mo	15	9	75
Intervention: Start GH 0.5 mg/m^2/d at 7 mo			
8 mo	33	28	57
Intervention: Hold GH at 8 mo			
Intervention: Adenotonsillectomy at 11 mo. FFL at 11 mo shows laryngomalacia			
12 mo	12	8	71
Intervention: Restart GH at 13 mo			
16 mo	44	30	61
Intervention: Hold GH at 16 mo			
22 mo	13	9	64
Intervention: Supraglottoplasty at 22 mo			
24 mo	8	6	72
Intervention: Restart GH at 27 mo			
30 mo	14	8	55

Abbreviations: AHI, apnea hypopnea index; oAHI, obstructive AHI; nO2, nadir oxygen saturation; mo, months; GH, growth hormone; FFL flexible fiberoptic laryngoscopy

Conclusions

- Respiratory difficulties can lead to significant morbidity in PWS
- Laryngomalacia is not well described in this population but can exacerbate OSA
- Growth hormone has significant benefit for infants with PWS but is monitored carefully due to concerns about aggravating OSA secondary to adenotonsillar hypertrophy
- Growth hormone may also unmask underlying laryngomalacia, possibly due to improved inspiratory force, which may require separate evaluation and treatment

Reference:

1. Tauber M, Diene G, Molinas C, Hebert M. 2008. Review of 64 cases of death in children with Prader-Willi syndrome (PWS). American journal of medical genetics Part A 146A(7):881-887.

Disclosure:

PS is involved in the multi-center study "A Randomized, Double-Blind, Placebo-Controlled Study of Diazoxide Choline Controlled-Release Tablet (DCCR) in Patients with Prader-Willi Syndrome" sponsored by Soleno Therapeutics, Inc.