Prevalent Sleep Disordered Breathing & Obstructive Sleep Apnea in Spite of Treatment for Acromegaly

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DISCLOSURES

• No conflicts of interest with respect to this presentation
Objectives

1. Describe the relationship of morphologic changes associated with acromegaly and the risk of sleep disordered breathing (SDB) or obstructive sleep apnea (OSA)
   - a. Define sleep disordered breathing and OSA
   - b. Define acromegaly
   - c. Outline overall risk factors for SDB and OSA
   - d. Outline morphologic changes that affect airway function in acromegaly
   - e. Identify co-morbid risks of OSA

2. Identify populations with OSA requiring further etiologic evaluation
   - a. Outline signs and symptoms indicative of risk
   - b. Select populations with OSA at risk for acromegaly
   - c. Outline co-morbidities of OSA in acromegaly

3. Explain rationale for re-screening male and female patients ‘cured’ of acromegaly for OSA
   - a. Demonstrate the use of screening tools in risk assessment for OSA/SDB
   - b. Argue for follow up sleep study for female patients ‘cured’ of acromegaly.

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Sleep Disordered Breathing:

- Episodic absence of breathing
- Oxygen saturation lower than 90%
Sleep Apnea

• **Central**- neural mediation of disordered or periodic breathing: injury, genetic autonomic dysfunction - etiology in brain stem

• **Obstructive**- repeated episodes of partial (hypopnea) or full (apnea) obstruction of the upper airway during sleep causing oxygen desaturation and brief arousal.

• **Mixed**
SDB and OSA- result in:

- Devita et al., 2016
- Silva et al., 2016
- Nutt et al., 2013
- Powlson & Gurnell, 2015
- Bilal, 2017

Diagram:

- Sleep Apnea
- Hypertension
- Obesity
- Drowsiness
- Fatigue
- Diabetes
- Impotence
- Depression
- Nocturia
- Mood
- Dementia & Memory Loss
- Lung Hypertension
- Stroke
- Headache
- Heart Attack
- Arrhythmia
- Motor Vehicular Accident
- Job Impairment
Acromegaly
Acromegaly:

- A pituitary adenoma which secretes excess growth hormone

- Rare -5 cases/million/year * prevalence is 60 cases/million

- Insidious average of 4-10 years to diagnosis (Melmed, 2009).

- Soft tissue and bony overgrowth.

- Cardiovascular mortality risk 4.6 times higher than that of the general population (Mestron et al., 2004; Sherlock et al., 2014).
Acromegaly & Sleep Apnea:

- Hypertrophy of pharyngeal soft tissue
- Craniofacial deformations
Macroglossia

Jaw & Joint deformities
Acromegaly & Obstructive Sleep Apnea:

40-80% 5%

Acromegaly General Population

OBS/OSA = Acromegaly
Acromegaly = OBS/OSA

(Galerneau et al., 2016).
Problem:

- Theoretically soft tissue hypertrophy is reversible post treatment (Powlson & Gurnell, 2015)

- Little data to support resolution of SDB/ OSA post normalization of growth hormone levels
AIM:

- To determine the prevalence of OSA by diagnosis versus those patients meeting risk criteria for SDB/OSA both pre and post treatment for acromegaly.
Methods:

- Prospective pre/post design
- Convenience sampling from a single institution

Inclusion Criteria

- New diagnosis of acromegaly (biochemical + pathology)
- Patients with & without Dx of OSA pre treatment

Exclusion Criteria:

- Other uncontrolled concomitant diseases
- History of nasopharyngeal surgery
Method:

• Patients without OSA diagnosis were evaluated by criteria for risk of OSA
  – StopBang questionnaire ( > intermediate risk)
  – Epworth Sleepiness Scale ( Score>10)

• All patients re-evaluated after surgical/ medically normalized growth hormone levels.

• Statistical analysis using PASW 18.
• IRB approved.
StopBang Questionnaire:

**S** - Snore loudly?

**T** - Tired, fatigued, or sleepy during daytime?

**O** - Observed no breathing?

**P** - High blood pressure?

**B** - Body Mass Index (BMI) more than 35?

**A** - Age over 50?

**N** - Neck circumference greater than 40cm?

**G** - Gender male?

**Low Risk** : Yes  0 - 2
**Intermediate Risk**: Yes 3-4
**High Risk**: Yes  5 - 8
Epworth Sleepiness Scale: Chance of Dozing (0-3)

1. Sitting and Reading
2. Watching TV
3. Sitting, inactive in a public place (e.g. a theater or a meeting)
4. As a passenger in a car for an hour without a break
5. Lying down to rest in the afternoon when circumstances permit
6. Sitting and talking to someone
7. Sitting quietly after lunch without alcohol
8. In a car, while stopped for a few minutes in traffic

0-10 = normal
Results: N=52

% Risk of OSA in Acromegaly Patients
Pre Treatment

- OSA-pre: 33%
- criteria: 39%
- No OSA: 28%
Demographics

<table>
<thead>
<tr>
<th>N=52</th>
<th>Pre treatment</th>
<th>Post Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>Males</td>
<td>23</td>
<td>29</td>
</tr>
<tr>
<td>Mean Age (years)</td>
<td>48</td>
<td>55.8</td>
</tr>
<tr>
<td>Dx OSA</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td># Meeting risk criteria</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Duration of follow up</td>
<td></td>
<td>66 months</td>
</tr>
<tr>
<td>Resolution</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>New diagnosis</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

* All patients meeting criteria referred for polysomnography
Results:

Post-treatment

- Linear by linear association indicated increasing age was associated with a higher likelihood of meeting criteria or having a diagnosis of OSA (p=0.04)

- OSA prevalence same for both genders pre treatment ($X^2$, p=0.19)

- Males were more likely to have a diagnosis of OSA after treatment for acromegaly (p=0.04).

- There was a significant reduction in the number of patients meeting risk criteria for OSA post treatment (P>0.001)

- There was no gender difference with respect to those meeting criteria for risk of OSA after treatment.
Post-operative Change in OSA

- Resolution of OSA
- New Onset OSA

Male
Female

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Prevalence of OSA Pre/Post Treatment for Acromegaly

- By Criteria Pre
- Pre Dx OSA
- By criteria post
- Post Dx OSA

17% Prevalence of OSA Pre/Post Treatment for Acromegaly
### Correlations:

<table>
<thead>
<tr>
<th>Male Gender</th>
<th>Post op OSA</th>
<th>$rs=0.3, p=0.04$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre OSA</td>
<td>Post op OSA</td>
<td>$rs=0.52, p=0.0001$</td>
</tr>
<tr>
<td>Higher Baseline IGF-1</td>
<td>OSA</td>
<td>$rs=-0.27, p=0.05$</td>
</tr>
<tr>
<td>Post Op IGF-1</td>
<td>OSA</td>
<td>$rs=0.7, p=0.6$</td>
</tr>
<tr>
<td>Post op Weight loss</td>
<td>OSA</td>
<td>$rs=0.2, P=0.2$</td>
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Conclusion

• Both males and females with acromegaly should be evaluated for sleep apnea
• A diagnosis of SDB or OSA may be a symptom of acromegaly particularly, in a young female
• SDB and OSA may persist post treatment for acromegaly despite normalization of growth hormone levels, particularly in males
• Some OSA risk factors such may resolve post treatment
• However, increasing age and BMI post treatment may be risk factors
• Validation in larger acromegaly patient populations recommended
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Thank you.

Questions?

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