Laryngeal Dystonia Gravidarum: Sudden Onset of Adductor Spasmodic Dysphonia in Pregnancy

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Objectives/Hypothesis: The purpose of this study was to identify the presence or absence of known factors related to onset of adductor spasmodic dysphonia (ADSD) in a population with sudden onset during or after pregnancy.

Study Design: Retrospective review.

Methods: A review of 350 patient records identified five patients with sudden onset of ADSD related to pregnancy. An age-matched group with sudden onset of ADSD not related to pregnancy served as controls. All subjects completed a 20-question survey of risk factors relevant to ADSD.

Results: The average age of onset in both groups was 31 years. Three had onset of ADSD in the postpartum period, the other two during pregnancy. Significantly increased avocational voice use was found in the pregnant group compared to the control group. There was a significant difference in the two groups regarding cumulative risk factors traditionally associated with ADSD.

Conclusions: Sudden onset of ADSD can occur in pregnancy in women with clinical profiles that differ from traditional ADSD patients.

Key Words: Adductor spasmodic dysphonia, pregnancy, sudden onset.

Level of Evidence: 3b

INTRODUCTION

Adductor spasmodic dysphonia (ADSD) is an idiopathic voice disorder that is characterized as a focal dystonia of the larynx.1,2 Patients with ADSD have uncontrolled, irregular contractions of the intrinsic laryngeal musculature, resulting in severe voice impairment. Onset is generally in the fifth decade of life and described as gradual. Spasmodic dysphonia is traditionally classified as adductor or abductor, although a mixed variant may exist. ADSD is characterized by hyperadduction of the vocal folds in connected speech, resulting in a strained and strangled voice quality and voice breaks.3 Abductor spasmodic dysphonia results from inappropriate abduction of the vocal folds in connected speech, causing breathy breaks in phonation.

ADSD results in significant impairment in functional communication. The disorder has no cure, and treatment is aimed at symptomatic management. Various treatments for ADSD have emerged over the years, including surgical methods such as recurrent laryngeal nerve section, and denervation-reinnervation surgery.4 At the present time, the most widely accepted form of treatment for ADSD is chemodenervation with botulinum toxin injection.1,4–8

Recently, Ludlow et al. have identified research priorities in spasmodic dysphonia.9 The need to characterize risk factors that may contribute to the onset of spasmodic dysphonia is among them. Ludlow et al. have broadly identified genetic factors, respiratory infections, and life stress as being factors associated with spasmodic dysphonia.9 A study by Tanner et al. explored risk factors in patients with ADSD compared to those with other voice disorders. Significant risk factors for ADSD included genetic and environmental factors such as past history of mumps, tremor, intense occupational and avocational voice use, as well as various elements in the patient’s family history.10,11 This suggests a multifactorial etiology of both endogenous and exogenous elements. A recent study by Childs et al. focused on patients with sudden onset ADSD and triggers associated with its development. Thirty-five percent of their patients with sudden onset of ADSD reported specific triggers to their disease onset such as stress and upper respiratory infection. This suggests that environmental factors may play a key role in the development of ADSD. Interestingly, 10% of the patients reported a sudden onset of ADSD related to pregnancy and parturition.12

Focal dystonias in pregnancy, termed dystonia gravidarum, have been reported. These cases have been few, self-limited, and none have been reported that involve the larynx.13–15 We sought to further explore the novel
**TABLE I.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at Onset of ADSD, yr</th>
<th>Pregnancy or Control</th>
<th>Timing of Onset During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35</td>
<td>Pregnancy</td>
<td>Postpartum</td>
</tr>
<tr>
<td>2</td>
<td>41</td>
<td>Pregnancy</td>
<td>Postpartum</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>Pregnancy</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>4</td>
<td>29</td>
<td>Pregnancy</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>Pregnancy</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>Control</td>
<td>N/A</td>
</tr>
<tr>
<td>7</td>
<td>42</td>
<td>Control</td>
<td>N/A</td>
</tr>
<tr>
<td>8</td>
<td>34</td>
<td>Control</td>
<td>N/A</td>
</tr>
<tr>
<td>9</td>
<td>42</td>
<td>Control</td>
<td>N/A</td>
</tr>
<tr>
<td>10</td>
<td>35</td>
<td>Control</td>
<td>N/A</td>
</tr>
</tbody>
</table>

ADSD = adductor spasmodic dysphonia; N/A = not applicable.

The development of ADSD in pregnancy does not follow the typical risk factor profile seen in traditional ADSD patients. The age of onset of ADSD is typically in the fifth decade, which differs significantly from the onset in the third and early fourth decades for patients developing ADSD in pregnancy. Over the course of two studies, Tanner et al. have asserted that 17 individual factors, such as a prior history of dystonia, viral infections including mumps, sinus infections, and a family association between pregnancy and laryngeal dystonia, as well as the risk factors prevalent in patients with sudden onset ADSD related to pregnancy and parturition.

**MATERIALS AND METHODS**

The institutional review board of Weill Cornell Medical College gave approval for this study. Using the same cohort of patients from a previous review of patients with sudden onset ADSD, clinical records, including initial visit notes, neurology, and speech pathology notes, from 2008 to 2010 were reviewed at an urban laryngology practice to identify patients with sudden onset of ADSD related to pregnancy, regardless of treatment status. From an initial group of 350 patients, 77 were identified as a sudden onset subgroup, and of those, five were of sudden onset during or immediately after pregnancy. Sudden onset was defined as onset over the period of 1 week. Additionally, age-matched control patients with sudden onset ADSD unrelated to pregnancy were selected from the above cohort. Patients were contacted and agreed to respond to a 20-question phone survey (see Appendix). The survey focused on personal and family history previously shown to be factors related to the onset of ADSD by Tanner et al. Analysis of the 20 items in the survey were compared between the pregnant and control groups using Pearson $r^2$ analysis. In addition, the total number of positive risk factors for each group was compared using a Mann Whitney $U$ test.

**RESULTS**

Three hundred fifty patients with ADSD were identified. Of these patients, five had sudden onset of ADSD related to pregnancy according to the criteria described earlier. The average age of onset of ADSD in the pregnant group was 32.4 years, with a range of 29 to 41 years. The average age of onset of ADSD in the control group was 36.6 years, with a range of 30 to 42 years (Table I). When compared to the control group, the only variable in the 20-question survey that achieved statistical significance was a history of significant avocational voice use in patients with ADSD related to pregnancy (0% vs. 60%, $P = .038$) (Table II). None of the other 19 variables, including viral illness prior to development of ADSD, a history of mumps infection, and family history of a voice disorder, individually showed a trend between the cases and controls.

Additionally, none of the patients had a history of rubella, blepharospasm, tremor, or obsessive-compulsive disorder.

The two groups were then compared with regard to the prevalence of the 17 risk and protective factors identified in the Tanner et al. studies. For this young group of 10 patients with ADSD, only 15 out of 85 possible occurrences of ADSD risk factors were present in the pregnant group, compared to 22 out of 85 in the control group (Mann-Whitney $U = 2.73, P < .05$). When examining the whole cohort as a group of young ADSD patients with sudden onset, 37 total risk factors for ADSD (21.8%) were present out of 170 possible occurrences. Of note, the viral-based factors (Table II, items 3, 4, 17) were more common in the nonpregnant group compared to the pregnant group.

**DISCUSSION**

The development of ADSD in pregnancy does not follow the typical risk factor profile seen in traditional ADSD patients. The age of onset of ADSD is typically in the fifth decade, which differs significantly from the onset in the third and early fourth decades for patients developing ADSD in pregnancy. Over the course of two studies, Tanner et al. have asserted that 17 individual factors, such as a prior history of dystonia, viral infections including mumps, sinus infections, and a family association between pregnancy and laryngeal dystonia, as well as the risk factors prevalent in patients with sudden onset ADSD related to pregnancy and parturition.

**TABLE II.**

<table>
<thead>
<tr>
<th>Increased risk of ADSD</th>
<th>ADSD Pregnant</th>
<th>ADSD Control</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hx of mumps</td>
<td>1/5</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td>2. Hx of rubella</td>
<td>0/5</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td>3. Hx of viral illness of voice</td>
<td>1/5</td>
<td>3/5</td>
<td></td>
</tr>
<tr>
<td>4. Hx of sinus infections</td>
<td>2/5</td>
<td>3/5</td>
<td></td>
</tr>
<tr>
<td>5. Hx of tremor</td>
<td>0/5</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td>6. Hx of blepharospasm</td>
<td>0/5</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td>7. Hx of dystonia</td>
<td>0/5</td>
<td>2/5</td>
<td></td>
</tr>
<tr>
<td>8. Hx of cancer</td>
<td>1/5</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td>9. Fam Hx of meningitis</td>
<td>1/5</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td>10. Fam Hx of voice disorder</td>
<td>0/5</td>
<td>1/5</td>
<td></td>
</tr>
<tr>
<td>11. Hx of OCD</td>
<td>0/5</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td>12. Hx of Tics</td>
<td>0/5</td>
<td>1/5</td>
<td></td>
</tr>
<tr>
<td>13. Hx of dust exposure</td>
<td>1/5</td>
<td>2/5</td>
<td></td>
</tr>
<tr>
<td>14. Hx of volunteer voice use</td>
<td>0/5</td>
<td>2/5</td>
<td></td>
</tr>
<tr>
<td>15. Occupational voice use</td>
<td>4/5</td>
<td>5/5</td>
<td></td>
</tr>
<tr>
<td>16. Avocational voice use</td>
<td>3/5</td>
<td>0/5</td>
<td>.038</td>
</tr>
<tr>
<td>17. Viral infection near onset</td>
<td>1/5</td>
<td>3/5</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>22</td>
<td></td>
</tr>
</tbody>
</table>

*Items taken from Tanner et al.

ADSD = adductor spasmodic dysphonia; Hx = history; OCD = obsessive-compulsive disorder.
history of voice disorders among others, impart an increased risk for the development of ADSD. Mumps, measles, and hepatitis vaccination appear to protect against the development of ADSD.10,11 Although these risk factors were significant in Tanner’s studies, our group of patients with ADSD related to pregnancy and the overall cohort of age-matched patients with ADSD had fewer of these factors. In addition, because only females were studied, it is possible that some of the risk factors previously reported2,10,11 may be related to males. Additional studies of spasmodic dysphonia may identify risk factors specific to various subgroups such as gender, age, or those with previous medical conditions. Items such as a history of rubella, blepharospasm, tremor, and obsessive-compulsive disorder were absent from our group of patients. However, a number of other factors were deemed significant in Tanner’s studies. Family history of voice disorders, dust exposure, prior history of dystonia, excessive avocational voice use, and viral infections were present in one or two patients in both the pregnant and control groups. When looking at both study and control patients together as a cohort of young patients with ADSD, it is clear that the overall group differs from the broader sample of ADSD patients in Tanner’s studies10,11 in that the present two groups were all female and were all under the age of 40 years. When comparing the pregnant and nonpregnant groups, the only risk factor that individually achieved statistical significance was a history of significant avocational voice use. This may represent additional vocal trauma that could predispose the patient to the development of vocal pathology, although spasmodic dysphonia is not regarded as a phonotraumatic disorder. We believe this represents an effect analogous to that found in musician’s dystonia, which is attributed to increased repetitive fine motor tasks as described by Frucht.16 The relationship to the acquisition of ADSD in pregnancy is of course not known. The pregnant and nonpregnant groups also differed when all 17 risk factors were considered together. Patients with sudden onset during pregnancy have fewer traditional ADSD risk factors than controls. The difference predominantly involves risk factors relating to viral infection, such as a past history of mumps, rubella, and viral illness near the onset of ADSD. These patients who develop ADSD in pregnancy may be a unique subset of young patients who develop ADSD. The difference in risk factor profiles suggests a different acquisition pathway or pathogenesis, much of which is unknown at this time.

Although the relationship of ADSD to pregnancy has not been reported previously, a number of neurologic disorders arise during or are exacerbated by pregnancy. Focal dystonias arising during pregnancy have been termed dystonia gravidarum. These cases all presented with symptoms of cervical dystonia early in the first trimester of pregnancy and spontaneously remitted after delivery.14,15 It has been postulated that rising levels of estrogen during pregnancy contribute to the onset of dystonia gravidarum due to alterations of central dopaminergic activity and dopamine receptor sensitivity in the basal ganglia.17,18 Susceptibility to dystonia gravidarum in individual women is hypothesized to be due to previously undetected basal ganglia pathology. It may be viewed as a “second hit” in an already susceptible system.

Along with dystonia gravidarum, myasthenia gravis (MG) and stroke have been related to pregnancy. During pregnancy, MG worsens in about one-third of patients and has an unusually unpredictable course.19 Stress related to pregnancy and varying levels of z-fetoprotein have been linked to the characteristic MG exacerbations and fluctuations, but the exact mechanism has not been elucidated20,21 Stroke is known to occur more frequently in pregnant women.22 The majority of these occur in the third trimester and puerperium and result from cerebral venous thrombosis, pre-eclampsia, and other hypertensive disorders. ADSD has not been understood as either a vascular or autoimmune event, so it is not clear that the above observations offer a way to explain its onset in pregnant women.

Schweinfurth et al.23 examined risk factors in 168 patients ranging in age from 13 to 71 years old. Although their data does not separate young from older or pregnant from nonpregnant subjects, they do show a higher incidence of patients with mumps and measles (65%) compared to those who did not have mumps or measles. The present data agree with Schweinfurth et al. but differ from the Tanner et al.11 data that found immunization was protective of ADSD.

Conclusions are limited by our small sample of patients with sudden onset of ADSD during pregnancy. However, this may represent the typical distribution of young patients with spasmodic dysphonia, as we initially derived our cohort from a larger group of 350 patients, of whom 177 had a sudden onset of spasmodic dysphonia. Nevertheless, larger cohorts of patients should be studied to further compare subpopulations (e.g., young versus elderly and men versus women) to identify risk factors related to ADSD as well as to abductor spasmodic dysphonia. Additionally, the questionnaires were administered long after ADSD onset and treatment and are subject to recall bias. Despite these limitations, we believe that this study demonstrates a difference between the risk profiles of young ADSD patients, some of whom attribute sudden onset of ADSD to pregnancy, and traditional ADSD patients.

CONCLUSION

Patients with sudden onset of ADSD in pregnancy represent a subgroup within a larger group of young patients who develop ADSD. These patients are more likely to be avocational voice users, but otherwise generally have fewer clinical risk factors as a whole when compared to traditional ADSD patients, suggesting pregnancy or a pregnancy-related change may be a risk factor in itself. Further studies surrounding the general pathogenesis of ADSD and the effect of estrogen on ADSD pathogenesis will aid in the understanding of this unique disease process.

APPENDIX

Adductor Spasmodic Dysphonia
Onset Questionnaire

Thank you very much for participating in this study on the onset of spasmodic dysphonia and its relationship
to pregnancy. Please answer the following about your history before the onset of spasmodic dysphonia. To the best of your knowledge:

1. Did you ever have the mumps? Y N
2. Did you ever have rubella? Y N
3. Did you ever have a viral infection affecting your voice? Y N
4. Have you ever been diagnosed with recurrent sinus infections? Y N
5. Have you ever been diagnosed with blepharospasm (rapid eye blinking)? Y N
6. Have you ever been diagnosed with a tremor? Y N
7. Do you have or have you ever been diagnosed with a focal dystonia other than ADSD (i.e., torticollis or writer's cramp)? Y N
8. Have you ever had cancer? Y N
9. Has anyone in your family had cancer? Y N
10. Does anyone in your family have, or did they have, a voice disorder? Y N
11. Have you ever been diagnosed with a compulsive disorder (i.e., obsessive-compulsive disorder, overeating)? Y N
12. Have you ever had a tic? Y N
13. Have you ever had extensive dust exposure? Y N
14. Was or is your occupation one that requires extensive use of your voice (i.e., teaching, sales, singing, acting)? Y N
15. Have you ever used your voice intensely in avocational situations (i.e., cheerleading, coaching, choral singing)? Y N
16. Do you or did you do volunteer work requiring extensive voice use? Y N
17. Did you have a viral infection near or at the onset of spasmodic dysphonia? Y N
18. Have you had the measles vaccine? Y N
19. Have you had the hepatitis vaccine? Y N
20. Have you had the mumps vaccine? Y N

BIBLIOGRAPHY