Grisel’s syndrome: The two-hit hypothesis—A case report and literature review

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Abstract
Grisel’s syndrome is a rare but well-documented clinical entity. It is a nontraumatic, fixed rotary subluxation of C1 on C2 (atlantoaxial). Although first described in 1830, the exact mechanism of Grisel’s syndrome remains unclear. We present a postoperative case of Grisel’s syndrome and an extensive literature review, and we propose a mechanism for its pathogenesis. In addition, we propose a treatment algorithm for Grisel’s syndrome.

Introduction
Grisel’s syndrome, previously described as a nontraumatic rotary subluxation of C1 on C2 (atlantoaxial subluxation) without any prior history of osteopathy, was first described by Bell in 1830 as a consequence of a syphilitic ulceration of the pharynx, but since has assumed the name of Grisel, a French otolaryngologist who described a similar syndrome following a course of nasopharyngitis in 1930. Grisel’s syndrome has been described in the otolaryngologic, neurosurgical, and orthopedic literature as a rare consequence of inflammatory, infectious, and/or postsurgical complication in the head and neck. Since its first description, the exact pathogenesis of Grisel’s syndrome has been the subject of much debate. No universally accepted mechanism for its occurrence exists, primarily because of the rarity of its presentation and its relative predilection for the pediatric population.

In this case report and literature review, we describe a case of Grisel’s syndrome and provide a critique of several proposed explanations for its pathogenesis. Finally, we provide a logical treatment approach based on our literature review.

Case report
An otherwise healthy 11-year-old boy underwent an uncomplicated tonsillectomy for recurrent tonsillitis. He had no history of trauma or preexisting bone disease. On postoperative day 3, the patient presented with increasing neck pain. There was no history of fever, chills, sweats, nausea, vomiting, or neurologic symptoms. The patient was evaluated and on physical examination was found to have a torticollis (chin down and to the left). Cervical range of motion was severely limited. There was no trismus. Intraoral examination revealed a normally healing surgical field. There was significant muscular spasm. A positive Sudeck’s sign was noted (spinous process of C2 displaced to the same side toward which the head is turned). Contrast computed tomography (CT) of the neck revealed a significant C1-C2 rotary subluxation (figure 1), consistent with a Fielding’s type 2 rotary subluxation. No abscess or significant lymphadenopathy was present.

The patient was immediately placed in a soft cervical collar, and a neurosurgical consult was obtained. He was treated with appropriate oral antibiotics, intravenous muscle relaxants, and bed rest. Three-dimensional computer-generated reconstructions derived from the CT scans of this patient were obtained, which further illustrate the C1-C2 subluxation (figure 2). Within 24 hours the patient’s torticollis resolved, as did the muscle spasm. CT and MRI scans performed on postoperative day 5 revealed complete resolution of the subluxation. The patient was maintained in soft cervical immobilization for 2 weeks, after which flexion-extension radiographs were obtained and found to be within normal limits. The collar was removed, and the patient did well with no lasting limitation or deficits.

Discussion
As previously noted, Grisel’s syndrome is a rare clinical phenomenon, primarily affecting the pediatric population, with 68% of patients under the age of 12 years and 90% under the age of 21. Depending upon how cases are categorized, they have been reported most commonly following surgical procedures in the head and neck (14 of 62, 22.6%), most often after mastoidectomy, tonsillectomy,
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and adenoidectomy, in that order. Upper respiratory infection was the second most commonly associated syndrome (12 of 62, 19.4%). Gourin et al reported 21 of 78 (26.9%) cases as postoperative complications, and 14 of 78 (18%) secondary to upper respiratory infection. There are no reports of predilection based on gender or predominance of the side affected.

Patients typically present with a painful torticollis, possible history of fever, and other nonspecific signs of infection. On physical examination, significant muscle spasm is evident, and patients typically have a fixed torticollis. A positive Sudeck’s sign is commonly observed. Although diagnosis of Grisel’s syndrome is clinical, confirmation of the diagnosis is radiographic. We feel that CT of the neck is the gold standard for diagnosis. The scan should be performed with contrast enhancement to rule out abscess formation. Although rotary subluxation can be diagnosed with plain radiographs, CT is more precise and is essential to rule out deep-space infection and abscess formation.

Grisel’s syndrome has been previously described, but its etiology is debated. Although several theories have been proposed, no mechanism for its pathogenesis has been generally accepted.

Grisel described the initial insult as inflamed, infected tissue surrounding the cervical spinal ligaments caused by an infectious process. The resulting spasm, with subsequent torticollis and subluxation, he hypothesized, was the body’s attempt to decompress the inflamed tissue. Although this theory is plausible, it does not account for the increased incidence of Grisel’s syndrome in children and does not propose a mechanism for the spread of infection or inflammatory mediators.

Others have proposed that an inflammatory process leads to a hyperemic state in the paravertebral tissues, causing a progressive decalcification of C1 and C2, and a subsequent weakening of the ligamentous insertions of the transverse ligament onto C1. Another hypothesis is that an inflammation-induced laxity of the cervical ligaments is the pathogenic key to Grisel’s syndrome. These proposals are supported by the work of Parke et al., who described a novel system of pharyngovertebral veins that drain the pharynx into the periodontal venous plexus. In a series of cadaver studies using latex injections, venous conduits were identified to be draining the nasopharynx and pharynx, ultimately to the periodontal venous plexus. In up to 50% of these specimens, venolymphatic anastomoses were identified. These conduits provide a pathway for a “septic effusion” to travel from the pharnyx to the stabilizing cervical spinal tissues.

Despite the existence of an anatomic pathway, in an extensive literature review, Pandya found no evidence that hyperemia and/or a septic infiltrate caused decalcification, ligamentous detachment, or ligamentous laxity. After an extensive MEDLINE search, we found only one study to support inflammation-induced ligamentous laxity, the mechanism proposed by Wittek and others. Lippmann provided invitro evidence of ligamentous laxity in response to inflammation. In that study, rabbit knees were injected with a turpentine solution to induce pyarthrosis. Ligamentous tensile strength was then evaluated in vitro in a controlled fashion and found to be significantly weakened. Although the pharyngovertebral venous plexus provides a pathway for infection and inflammatory mediators to reach the cervical ligaments, no other evidence supports ligamentous weakening or laxity induced by inflammation. In a variation of the previously mentioned proposals, Boiten et al suggested that the initial inflammatory hyperemia
represented a critical phase, which if treated promptly was reversible but if untreated led to weakening and laxity of the cervical ligaments, possibly causing subluxation.

We propose a two-hit hypothesis. The first “hit” is a preexisting cervical ligamentous laxity seen in the pediatric population at baseline. Jackson, among others, noted a hypermobility of C1 on C2 in children, as manifested by an increased atlas-dens interval. The normal adult interval ranges from 2.5 to 3 mm; in children, this interval may be as great as 4.5 mm. A convincing argument can be made that children are at increased risk based on this hypermobility. In a second “hit,” inflammatory mediators carried to the cervical muscles by the pharyngovertebral plexus induce spasm and subsequent subluxation. Several arguments support this model of pathogenesis. First, there is a convincing anatomic pathway for the transport of inflammatory mediators. Second, the muscular response to inflammation is spasm and tightening. Finally, children, who are most frequently affected by Grisel’s syndrome, have a known preexisting laxity of the stabilizing ligaments of C1 and C2, specifically the transverse ligament. The following question must then be asked: Why doesn’t Grisel’s syndrome occur more frequently? Simply put, not every child has hypermobility of the C1-C2 joint (i.e., not every child would display an increased atlanto-dens interval radiographically).

Although the majority of patients with Grisel’s syndrome recover without lasting functional or neurologic deficit, there is the potential for severe, even catastrophic, consequences if patients are misdiagnosed or mistreated. Most case reports describing lasting or catastrophic effects cite a significant delay in diagnosis, with a mean delay of 11.6 months. Although these reports are not recent, they highlight the importance of early diagnosis and prompt, proper treatment. The literature cites many cases of Grisel’s syndrome that resolve with no lasting deficit after fairly aggressive treatment (cervical traction, halo immobilization). The following question must then be asked: Why doesn’t Grisel’s syndrome occur more frequently? Simply put, not every child has hypermobility of the C1-C2 joint (i.e., not every child would display an increased atlanto-dens interval radiographically).

In conclusion, Grisel’s syndrome is a rare clinical entity that may be seen in a variety of clinical settings. Every otolaryngologist should be familiar with its epidemiology, presentation, and management. It is our theory that children who have a hypermobility of C1 on C2 are at risk for Grisel’s syndrome following any kind of inflammatory, infectious, and or postoperative process in the head and neck. Patients with Grisel’s syndrome can have catastrophic outcomes, but prompt diagnosis and proper treatment significantly improve the chances for full functional recovery.

Table. The Fielding classification of rotary subluxation

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<thead>
<tr>
<th>Type  1</th>
<th>Rotary fixation with no anterior displacement, with odontoid acting as the pivot point.</th>
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<tr>
<td>Type 2</td>
<td>Rotary fixation with anterior displacement of 3-5 mm, one lateral articular process acting as the pivot.</td>
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<tr>
<td>Type 3</td>
<td>Rotary fixation with anterior displacement of &gt;5 mm.</td>
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<tr>
<td>Type 4</td>
<td>Rotary fixation with posterior displacement.</td>
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aggressively, as should cases of chronic subluxation that are not improved with appropriate therapy. We also feel that prompt neurosurgical consultation is indicated if the diagnosis of Grisel’s syndrome is suspected. The point to be stressed is that prompt, individualized treatment is essential for full functional recovery.

References