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REVIEW ARTICLE

Pediatric glossopharyngeal neuralgia: a comprehensive review

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ABSTRACT

Introduction Debilitating facial pain can seriously affect an individual's daily living. Given that the pathophysiology behind neuropathic and myofascial pain is not fully understood, when chronic facial pain goes undiagnosed, it has been proposed that one of the two is the likely cause. Since their discovery, glossopharyngeal neuralgia (GN) and Eagle's syndrome have been considered mostly conditions afflicting the adult population. However, when pediatric patients present with symptoms resembling GN or Eagle's syndrome, physicians are less apt to include these as a differential diagnosis simply due to the low prevalence and incidence in the pediatric population.

Materials and methods A literature review was performed with the aim to better understand the history of reported cases and to provide a comprehensive report of the anatomical variations that lead to these two conditions as well as the way these variations dictated medical and surgical management. Articles were obtained through Google Scholar and PubMed. Search criteria included key phrases such as pediatric glossopharyngeal neuralgia and pediatric Eagle syndrome. These key phrases were searched independently. PubMed was searched primarily then cross-referenced articles were found via Google Scholar. Results from non-English articles were excluded.

Results A total of 58 articles were reviewed. Most of the articles focused on adult glossopharyngeal neuralgia, and the majority was comprised of case reports. When searched via PubMed, a total of 16 articles and 2 articles returned for glossopharyngeal neuralgia and Eagle's syndrome, respectively. After criteria selection and cross-referencing, a total of seven articles were found with respect to pediatric glossopharyngeal neuralgia.

Conclusions While they are rare conditions, there are multiple etiologies that lead to the debilitating symptoms of GN and Eagle's syndrome. The clinical anatomy proved notable as multiple causes of GN and Eagle's syndrome are due to variation in the anatomy of the neurovascular structures surrounding the glossopharyngeal nerve, an elongated styloid process, a calcified stylohyoid ligament as well as a calcified stylomandibular ligament. Due to the success of different treatment modalities, the treatment of choice is dependent on clinical judgment.

Keywords Myofascial pain · Neuropathic · Trigeminal neuralgia · Glossopharyngeal neuralgia · Eagle's syndrome · Gamma knife radiosurgery (GKRS)

Abbreviations

GN	Glossopharyngeal neuralgia
TN	Trigeminal neuralgia
PICA	Posterior inferior cerebellar artery

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Introduction

Debilitating facial pain can seriously affect an individual's daily living. Given that the pathophysiology behind neuropathic and myofascial pain is not fully understood, when chronic facial pain goes undiagnosed, it has been proposed that one of the two is the likely cause [9]. Of the neuralgias, trigeminal (TN), glossopharyngeal (GN), and occipital neuralgia are the three that have been researched the most to date, with the majority of the literature focused on TN. A large-scale population-based study in Germany reported the prevalence of TN to be 0.3% [38]. In another cohort study that compared the rates of TN to GN, the occurrence for TN was found to be lower than that of the one in Germany, but still the ratio of occurrence for TN to GN was 5.9:1 [26] reflecting that, of the neuralgias, TN occurs at a greater frequency than GN. Occipital neuralgia's true prevalence is not yet known, and to complicate things further, studies have shown that convergence of cervical afferent fibers can occur with trigeminal nerve fibers leading to ocular as well as occipital pain, suggesting it may be more difficult to ascertain the prevalence [49, 51, 52].

While there is less research on GN compared to TN, there is even less information with regard to pediatric GN [1, 7]. In the retrospective cohort study that compared TN to GN, a total of 12 cases were found in a population of 70,000 over the 40-year period [26]. While the results revealed a low prevalence of GN, the study was not specific to pediatric cases and the average age. The data to reflect the prevalence of GN from the general population is limited, not to mention the data concerning GN in the pediatric population being sparse as well. Since its discovery in the pediatric population, there have been cases of GN reported revealing associations with multiple syndromes and malformations, with the most common association belonging to Eagle's syndrome [47]. This being said, there exist no large-scale studies to reveal the prevalence of Eagle's syndrome within the pediatric population. As a result, it is our goal in this study to review the current literature with respect to GN and the associated Eagle's syndrome in the pediatric population. We aim to better understand the relevant variations in anatomical causes of GN and Eagle's syndrome, the total number of cases, and the different management modalities reported thus far.

Methods

Articles were obtained through Google Scholar and PubMed. Search criteria included key phrases such as the following: pediatric glossopharyngeal neuralgia and pediatric Eagle syndrome. These key phrases were searched independently. PubMed was searched primarily; then, cross-referenced articles were found via Google Scholar. Results from non-English articles were excluded. Articles that mentioned palsy or cranial nerve impairment were evaluated for associated neuralgias; those not reporting a neuralgia were excluded. When relevant clinical information was missing from the literature concerning pediatric glossopharyngeal neuralgia, results and data from cross-referenced articles with respect to adult glossopharyngeal neuralgia were used in their stead.

Results

A total of 58 articles were reviewed. Most of the articles focused on adult glossopharyngeal neuralgia and the majority

Table 1 GN

Study type/year	Age/sex	Cause of GN	Treatment	Outcome	Unique finding
Case study/2016	22/M 9 at onset of symptoms*	Neuropathic following radiation and platinum-based chemotherapy treatment for neuroectodermal tumor	Prednisone	Unknown	Bilateral GN
Case study/2015	10/M	C1 malalignment	Chiropractic	Asymptomatic at 1.5 years after treatment	Only chiropractic treated case reported
Literature review and Case study/2015	5/M	Unknown	Multiple pharmacologic agents; treatment still unsuccessful	Still symptomatic at last follow-up	Associated with red ear syndrome*
Comprehensive review/2012—Dubey	Multiple	Multiple	Multiple	Multiple	Covers previous case reports, uses adult neuralgia statistics
Comprehensive review: Headaches and neuralgias/2003—Kondov	Unknown	Multiple	Multiple	Multiple	Covers two of the discussed cases
Case report/2000	13/F	Looping R. PICA	Gabapentin	Unknown	———
Case report/1996	8/F	Chiari malformation type 1	Surgical decompression	Asymptomatic at 2-year follow-up	Associated with Arnold Chairi type 1

*The case report concerning red ear syndrome in a 5-year-old male did not specifically state a diagnosis of GN, but did describe the patient's symptoms which sounded typical of GN were comprised of case reports. When searched via PubMed, a total of 16 articles and two articles returned for glossopharyngeal neuralgia and Eagle's syndrome, respectively. After criteria selection and cross-referencing, a total of seven articles were found with respect to pediatric glossopharyngeal neuralgia. One article associated with red ear syndrome did not mention an actual diagnosis of GN but was included as there is an association between the two and the patient described symptoms consistent with GN. Of the glossopharyngeal neuralgia articles, two were reviews of the current literature and the remaining 4 were case reports. After criteria selection and cross-referencing, a total of six articles were found with respect to pediatric Eagle's syndrome. One of the articles for Eagle's syndrome was in Spanish and the data/results from this study were excluded from this review. There was a retrospective cohort study that evaluated panoramic graphs of a specific population and found elongated styloid processes in the pediatric population; however, no description of symptoms was provided; thus, this study was excluded. The four remaining articles were case reports. The rest of the articles used for the review were cross-referenced from these articles resulting in the total 40 articles cited within this review.

Table 1 summarizes the findings from the pediatric studies for glossopharyngeal neuralgia and Eagle's syndrome.

History

The first case of GN was reported in 1910 by Weisenberg. The patient had presented with lancinating pain of the throat and ear that was initially mistaken for tic douloureux [43]. In 1921, Harris described a syndrome which presented with severe, paroxysmal, unilateral pain that was also lancinating in character. The pain would begin in the tonsillar region and anterior pillar of the fauces and then radiate to the ear, mandible, and upper part of the neck. Given the pain was distributed through the avenue of the sensory fibers for the glossopharyngeal nerve, the term glossopharyngeal neuralgia was coined [14]. It was around 70 years later that the first pediatric case was reported [25], except for a retrospective cohort study that reported the youngest age of a patient suffering from GN being 16 [45].

Epidemiology

As previously mentioned, large-scale studies to determine the overall incidence and prevalence of GN in the pediatric population are lacking. However, in the year 1991, a retrograde cohort study mentioned earlier the overall incidence rate of GN in the general population was reported as roughly 12 per 100,000 individuals, reaffirming that GN truly is a rare condition. The same study went on to note that incidence increased with age, suggesting that the incidence rate for the pediatric population is even lower than that for the general population [26].

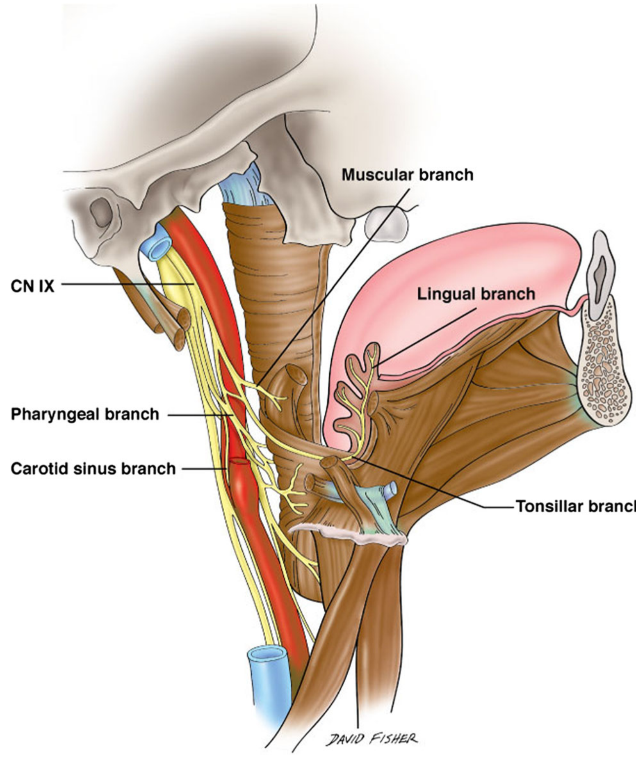

Fig. 1 Branches of the glossopharyngeal nerve

Anatomical significance

Figure 1 demonstrates the branches of the glossopharyngeal nerve. Dependent on the area afflicted, pain can essentially travel along any of the sensory segments for these branches. Note the proximity of the styloid process as well as the internal carotid (branches have been removed for visualization of the glossopharyngeal nerve) which reflects the possibility of these structures compressing the nerve and causing the symptoms of GN.

Signs, symptoms, and presentation for GN in the pediatric patient

Pediatric patients with GN suffer from the same symptoms as adults: severe and lancinating pain that is paroxysmal and episodic in occurrence. However, in the pediatric patient, there seems to be a scarcity of pain-free episodes as well as an exaggerated response [9]. Triggers for the episodes are typically yawning, chewing, swallowing, or in some cases eating certain types of food [9, 10]. The pain is usually unilateral, though there have been descriptions of bilateral occurrence in young adults [15]. Depending on the etiology of GN, individuals may also present with palatal paralysis as well as headaches; however, the patient's headache may more likely be attributed to an underlying etiology that is responsible for both [29, 57]. Two main presentations have been described based on the location of the pain: peritonsillar or deep in the ear [9]. Because of these distributions, patients may suffer from odynophagia secondary to GN [9]. Thus, the daily living for a pediatric patient that suffers from chronic glossopharyngeal neuralgia can be severely affected, to the point of malnutrition and developmental delay [8, 9, 29, 34]. In addition, reports have shown that children and young adolescents with chronic facial pain are prone to suffer from psychiatric illnesses such as depression and anxiety [9]. While the presentation of GN remains relatively stable across the board, the management is more dependent on the etiology.

Diagnosis

The diagnosis for GN is strictly clinical. In 2013, the International Classification of Headache Disorders devised diagnostic criteria for GN which include the following: at least three pain attacks in regions of GN distribution (posterior tongue, tonsillar fossa, pharynx, beneath the angle of the jaw, and/or in the ear); three or more of the following characteristics, paroxysmal pain attacks that are recurrent, duration of a few seconds to 2 min, severe pain that is shooting and stabbing in nature, precipitated by swallowing, coughing, talking, or yawning; no neurological deficits; pain cannot be accounted for by another neurological diagnosis according to ICHD [1].

Etiologies and their management

Essentially, anything that compresses or damages CN IX and/or its branches can cause symptoms of GN. Often, the cause is unknown [9]. Of the known causes, the most common include neurovascular compression/vascular variations and pathologies (i.e., vertebral artery dissection), tumors, infection, infarction, and trauma [9]. In 2000, Childs et al. published a case report with a 13-year-old girl who experienced GN as a result of a looping posterior inferior cerebellar artery (PICA). After the initial magnetic resonance imaging was found to be inconclusive, MRA revealed a looping right PICA that was compressing cranial nerves IX and X as they exited the upper medulla [6]. Initial pharmacological therapy with carbamazepine provided little relief leading to the therapeutic drug being switched to gabapentin, which drastically improved the patient's symptoms and omitted the need for microvascular decompression (MVD)—the major surgical technique for vascular compression of CN IX [6]. This case reflects a reasonable approach to management; however, Childs et al. fail to mention any follow-up with the patient. While the type of management is typically a matter of preference, the degree of compression, efficacy of pharmacotherapy, and amount of pharmacologic side effects all impact a physician's decision. At the time of their study, Childs et al. noted a lack in literature of large-scale studies for the long-term use of the antiepileptics while managing pediatric neuropathy [6]. Currently, the general principle of maximizing attempts at pharmacotherapy prior to surgical intervention is the recommended practice, and pharmacotherapy has proven to be an effective treatment in about a third of the cases reported [6, 9, 15].

In addition to a lack of studies that observe the long-term effects of antiepileptics in GN, there are few controlled studies available to determine the most beneficial medication in treating pediatric neuralgias in general [53]. Currently, antiepileptics and antidepressants are the two major classes of first-line treatment for GN. A 2006 review of the non-epileptic use of antiepileptics in children showed there were no trials evaluating the safety and/or efficacy of these medications [11]. Since then, there have been numerous reports of beneficial treatments for specific cases of neuropathy [53], but no study with enough power to develop guidelines. Treatment is currently chosen via trial and error based on the current recommendations for adults, and physicians typically try a few different classed neuropathic pain medications before attempting alternative treatments.

While certain surgical treatments have shown more permanent benefits for the patient, surgery is still reserved for those suffering from GN refractory to medical treatment, those who failed previous operative treatment, and those who are intolerant to adverse effects of medications. The preferred surgical approach for GN secondary to neurovascular compression has been MVD. Interestingly, studies have shown that pediatric patients suffering from TGN do not respond as well to this surgical technique when compared to the adult population [43]. However, results concerning MVD efficacy for GN in the pediatric population were not mentioned [43]. There has been a report of successfully treating pediatric GN associated with Chiari malformation via surgical decompression [55]. Transcervical resection of the glossopharyngeal nerve and pulsed radiofrequency are other modalities of treatment for GN that have been seen to show positive results [25].

A new technique that may replace MVD is gamma knife radiosurgery (GKRS). GKRS has shown positive results including better pain control and lower complications rates when compared to MVD and other forms of ablation [48, 56]. However, in their study, Spina et al. noted that the best candidates for gamma knife radiosurgery were individuals > 70 years of age [48]. Other than this study, there is no data to suggest that GKRS will be effective for the treatment of GN in the pediatric population. GKRS has already shown to be beneficial for ablation of various pediatric tumors as well as arteriovenous malformations [32, 54, 58]. When more information concerning long-term efficacy and prognosis for this technique with respect to managing GN is obtained, it may eventually replace MVD as the preferred surgical technique.

Eagle's syndrome

In the mid to late 1930s, WW Eagle described what is now termed Eagle's syndrome and attributed this disease to an elongated styloid process or calcified stylohyoid ligament. Eagle deduced that elongation of the styloid process or calcification of the stylohyoid ligament causes impingement upon the glossopharyngeal nerve resulting in the symptoms [46]. Eagle went on to classify the extent of calcification as well as the affected segments, and claimed that the symptoms of Eagle's syndrome would occur post-tonsillectomy because of scar tissue formation around the styloid apex [46]. Since then, there have been numerous reports of patients suffering from Eagle's syndrome who have never undergone a tonsillectomy. As a result, there have been multiple proposals to include other causes of Eagle's syndrome such as the following: ossification of the stylohyoid ligament complex resulting in contraction of strap muscles of the neck which in turn stretch the glossopharyngeal nerve, a fractured calcified stylohyoid ligament that forms excessive granulation tissue, abnormal angulation of the styloid process, and ossification of muscular tendons of nearby structures [2, 30, 35, 36, 50].

While there is literature with regard to Eagle's syndrome in the adult population, the literature concerning pediatric Eagle's syndrome is lacking [13]. A recent retrospective analysis of over 600 patients' panoramic digital grafts revealed an occurrence of an elongated styloid process in 33% of the group, with the pediatric population comprising only 6% of that one-third [12]. In one of the most recent reports of pediatric Eagle's syndrome, Garriz-Luiz noted a total of four cases previously reported in the literature [13]. In their study, Gracco et al. provided the most recent comprehensive data for the occurrence of Eagle's syndrome in the general population [12]. This study reflects a low prevalence for Eagle's syndrome in the pediatric population; however, more comprehensive work focused on pediatric Eagle's syndrome would be beneficial to ascertain the true prevalence amongst pediatric patients.

In 2002, a report given by Slavin et al. deemed the presentation of pain in Eagle's syndrome as more constant and dull in character when compared to GN [47]. However, Slavin et al.'s study was a case report limited to the experience of one 38-year-old female. As previously mentioned in one of the more recent works that focuses on the pediatric population, Dubey et al. claim that in the pediatric population, GN typically is a more constant pain [9]. Thus, it would be reasonable to deduce that pediatric Eagle's syndrome is more constant than adult Eagle's syndrome and pediatric glossopharyngeal neuralgia; however, more cases need to be reviewed before this assumption can be validated.

In addition to the diagnostic clinical picture, the limited cases of pediatric Eagle's syndrome reported so far seem to prefer panoramic radiographs over two-view radiographs as these allow complete visualization of the styloid process [12, 13]. In 2015, Kent et al. suggested that the diagnostic criteria for Eagle's syndrome should be attributed to the distance between the tip of the styloid process to the tonsillar fossa [28]. In their study, they found that there was significant difference between patients who had a shorter distance between the styloid process and the tonsillar fossa irrespective of the length of the styloid process [28]. Kent also recommended the use of CT scans as more accurate when diagnosing Eagle's syndrome and planning management. Eagle's syndrome is also currently

Table 2 Findings from the pediatric studies for Eagle's syndrome

Study type/year	Age and sex	Cause of Eagle's syndrome	Treatment	Outcome	Unique finding
Case study/2017	12/M	Right-sided elongated styloid process and calcified stylohyoid ligament	Partial ablation of the calcified stylohyoid ligament and shortening of styloid process	Residual pain for 1 year complication of anxiety post op. After the first year, patient remained asymptomatic for the remainder of his childhood	————
Case study/2001	11/F	Calcification of the both right and left stylohyoid ligaments	Transection of the stylohyoid ligament	Asymptomatic at 1-year follow-up	Bilateral calcifications of the stylohyoid ligament.
Case study/1990	5/F	Calcification of the stylomandibular ligament	Reassurance Antibiotics for concomitant chronic sinusitis	Unknown	Dysphagia and cough instead of pain. Calcified stylomandibular ligament was found
Case study/1986	13/M	Right elongated styloid process	2 procedures 1X GN resection 1X styloidectomy	Asymptomatic at 2-year follow-up after styloidectomy	First recorded case of pediatric Eagle's syndrome

diagnosed via reproducible pain upon palpation of the tonsil or tonsillar fossa and alleviation of that pain with the use of anesthetics afterwards [37]. Again, these studies were done on the general population and did not focus on pediatric patients. So far, the four case reports provided in this review for pediatric Eagle's syndrome have been diagnosed via multiple imaging techniques regarding clinical picture; Holloway et al. diagnosed Eagle's syndrome from lateral radiographs while the more recent reports provided by Quereshy et al. and Grazzi-Luiz used panoramic radiographs and 3D CT visualization, respectively [13, 17, 42].

Current management for Eagle's syndrome in general includes both conservative and non-conservative methods, like the management of glossopharyngeal neuralgia. The main exception is that in Eagle's syndrome, the surgical approach is more concerned with removal of the styloid process as opposed to decompression or resection of the nerve [2, 12, 28]. Like in most neuralgias, similar medications used (antiepileptics, antidepressants, and antipsychotics) have been shown to be more effective than analgesics in the few cases that have been reported thus far for Eagle's syndrome in general; however, in three out of the four pediatric cases included in this review, they resulted in surgery. These findings are summarized in Table 2.

Although cranial nerve neuralgias are often undiagnosed in children, the clinician should be aware of this anatomy and potential variations how these might contribute to pathology [3–5, 7, 16, 18–24, 27, 31, 33, 39–41, 44]. A better understanding of such morphology can improve patient care and treatment strategies.

Conclusion

GN and the associated Eagle's syndrome have been documented in the population since the early twentieth century. Most of cases reported and studies performed thus far focus on the adult population with many reports reflecting the average age to be above 30. When pediatric patients present with symptoms indicative of GN or Eagle's syndrome, physicians may dismiss these diagnoses as their incidence amongst the pediatric population is rare. This literature review was performed to provide a summary of the reported cases for GN and Eagle's syndrome in the pediatric population. While they are rare conditions, there are multiple etiologies that lead to the debilitating symptoms of GN and Eagle's syndrome. The clinical anatomy proved notable as multiple causes of GN and Eagle's syndrome are due to variation in the anatomy of the neurovascular structures surrounding the glossopharyngeal nerve, an elongated styloid process, a calcified stylohyoid ligament as well as calcified stylomandibular ligament. Due to the success with different treatment modalities, the treatment of choice is dependent on clinical judgment, though most attempt conservative methods prior to surgery. We hope these findings will help bring awareness to these diagnoses at time of presentation and the anatomical descriptions of variant structures help guide physicians in deciding management.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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