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ANATOMIC VARIATIONS

Extracranial hypoglossal neurofibroma with a variant ansa cervicalis: a case report

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Abstract

Purpose This case report aims to explore a rare combination of findings in a cadaver donor: variant ansa cervicalis, vagus (CN X) and hypoglossal (CN XII) nerve fusion, and extracranial hypoglossal neurofibroma.

Background The type of ansa cervicalis variation presented in this report has been documented in less than 1% of described cases. The CN X-CN XII fusion has been reported in one prior study. Additionally, hypoglossal neurofibromas are benign neoplasms of the peripheral nerve sheath. There are only two known cases of extracranial hypoglossal neurofibroma described in the literature.

Case report The study investigated a swelling of the right CN XII in a 90-year-old female cadaver donor. Detailed dissection, examination of the region, and histopathological analysis of the mass followed. The entire course of CN XII and other cranial nerves were examined to exclude concurrent pathology. A fusiform enlargement of the right CN XII was observed in the submandibular region, measuring ~ 1.27 × 1.27 cm. The superior portion of the right CN XII was fused to the right CN X, exiting the jugular foramen. The superior root of ansa cervicalis, normally a branch of CN XII, was found to arise from CN X on the right side. The left CN XII and CN X were unremarkable. Histopathological examination revealed benign neurofibroma.

Conclusion The anatomical variation and rare location of the tumor necessitate further investigation to better understand pathogenesis, clinical correlation, and surgical implications. This study furthers knowledge of this condition and contributes to the currently limited body of research.

Keywords Extracranial neurofibroma · Neurofibroma · Ansa cervicalis · Anatomical variation

Introduction

The ansa cervicalis, located superficial to the carotid sheath within the carotid triangle of the neck, is a nerve loop arising from cervical nerve roots C1, C2, and C3 [3]. This loop connects the superior root (C1) with the inferior descending root (C2, C3) of cervical spinal nerves and innervates the infrahyoid muscles, which primarily function to preserve phonation and deglutition [3, 5]. Typically, the superior root of the ansa cervicalis is derived from C1 nerve fibers branching off the hypoglossal nerve [5]. Variation in composition and course of the ansa cervicalis is more commonly seen among inferior roots [5]. However, this case report describes a unique combination of findings in which the hypoglossal and vagus nerves are fused upon exiting the jugular foramen, thereby giving rise to a rare variation of the ansa cervicalis in which the superior root of the ansa branches solely off the vagus nerve. While the vagus nerve and hypoglossal nerve typically exit the skull separately via the jugular foramen and hypoglossal canal, respectively, only one other case has been identified whereupon the vagus nerve and the hypoglossal nerve are fused with the ansa cervicalis arising from the vagus nerve [9, 11]. Furthermore, this type of ansa cervicalis variation often referred to as a type IV vagal ansa under the Jelev classification system, has been estimated to occur in less than 1% of reported cases [3]. Although usually asymptomatic, awareness of possible anatomic variation of the ansa cervicalis becomes especially important during surgery of the head and neck, particularly for surgeons who perform laryngeal reinnervations [3, 9, 11].

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Additionally, this case report presents an extracranial hypoglossal neurofibroma. Hypoglossal neurofibromas are rare, slow-growing, benign neoplasms of the peripheral nerve sheath consisting of Schwann cells, perineurial cells, and fibroblasts [7]. Most neurofibromas occur sporadically, with 10% of cases associated with Neurofibromatosis type 1 (NF-1), an autosomal dominant disorder [1, 7]. Literature suggests that only 5% of neurogenic tumors in the neck arise from the hypoglossal nerve, with most of these being Schwannomas [1, 7]. Further, it has been found that hypoglossal tumors are more frequently intracranial, with extracranial extension occurring in 30% of cases [1, 7]. The combination of these statistics makes this case exceedingly rare, as only two cases have been documented as purely extracranial hypoglossal neurofibroma in the literature [2, 7]. The purpose of this report is to explore the rare combination of ansa cervicalis variation, vagus-hypoglossal nerve fusion, and extracranial hypoglossal neurofibroma. This case highlights the importance of documenting and understanding the relationship of ansa cervicalis variants with surrounding anatomical structures, especially in the context of maximizing surgical outcomes.

Case report

A 90-year-old female donor was examined during routine dissection in a medical school anatomy laboratory. The donor's cause of death was Alzheimer's disease. Initially, a swelling of the right hypoglossal nerve was noticed while dissecting the carotid triangle. Detailed dissection and thorough examination of the region followed to further investigate this finding. The entire course of hypoglossal nerves and other cranial nerves were examined bilaterally, both intracranially and extracranially, to exclude concurrent pathology. Photographs of the mass and the entire course of the right hypoglossal nerve were taken. The dimensions of the tumor were measured using digital calipers. After documentation, researchers carefully removed the mass for biopsy and sent the specimen to a pathology laboratory for analysis. A histopathological examination of the tumor was performed using hematoxylin and eosin staining techniques. Photographs of microscopic images were taken, and a pathologist was consulted.

A fusiform enlargement of the right hypoglossal nerve was observed in the submandibular region. It measured approximately 1.27×1.27 cm (Fig. 1a). Concurrently, researchers found the superior portion of the right hypoglossal nerve fused to the right vagus nerve (Fig. 1b). The right hypoglossal nerve, which usually leaves the skull through the hypoglossal canal, was found fused at its exit to the right vagus nerve that emerged from the jugular foramen. Additionally, the superior root of the ansa cervicalis, normally a branch of the hypoglossal nerve, was found to arise from the vagus nerve on the right side. Meanwhile, the left hypoglossal and vagus nerves appeared unremarkable. No other tumors were noted, nor was any other anatomical variation present along other cranial nerves on either side. Histopathological examination and special staining revealed the tumor to be a benign neurofibroma (Fig. 2).

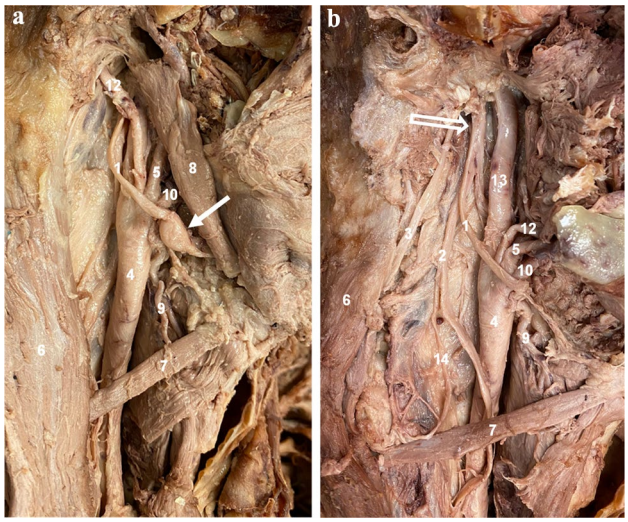

Fig. 1 **a** Right carotid triangle showing the tumor and its relations. **b** Right carotid triangle showing the variant ansa cervicalis and its relations. 1. Hypoglossal nerve, 2. Vagus nerve, 3. Accessory nerve, 4. Common carotid artery, 5. External carotid artery, 6. Sternocleidomastoid, 7. Superior belly of omohyoid, 8. Posterior belly of digastric, 9. Superior thyroid artery, 10. Common trunk of lingual and facial arteries, 12. Occipital artery, 13. Internal carotid artery, 14. Superior root of Ansa Cervicalis, Open arrow: Fused Hypoglossal and Vagus nerves, Closed arrow: Neurofibroma

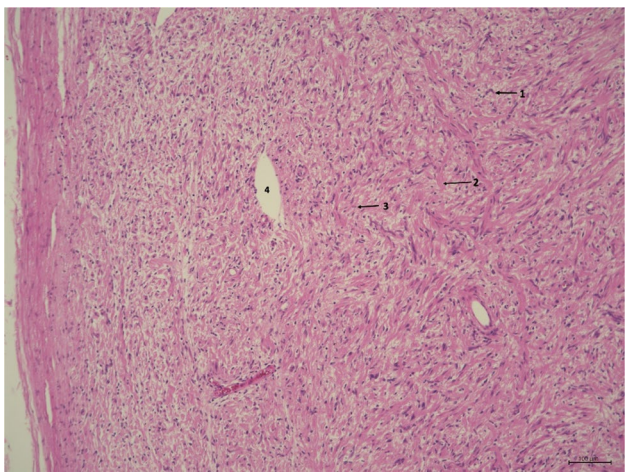

Fig. 2 Hematoxylin and Eosin staining reveals localized (sporadic) neurofibroma with neoplastic Schwann cells (1), abundant collagen fibers (2), scattered fibroblast (3), and venules (4)

Discussion

Ansa cervicalis

The ansa cervicalis is a neural loop with two roots located in the neck that innervates the infrahyoid muscles. This neural loop consists of a superior root from cervical spinal nerve C1 and an inferior root comprised of nerve fibers from the ventral rami of C2-C3 [5]. In typical ansa cervicalis formation, the fibers arising from cervical spinal nerve C1 course along the hypoglossal nerve and then descend from the hypoglossal nerve as the superior root of the ansa cervicalis [5]. Several variations of both the formation and course of the ansa cervicalis have been reported and categorized [9]. The variations in the formation of the ansa cervicalis are grouped into five broad categories by Jelev's Classification (Fig. 3). In Type I, there is no superior root formation of the ansa cervicalis. Type II is typical ansa cervicalis formation with the ansa cervicalis branching off the hypoglossal nerve. Type III variation consists of C1 fibers branching off both the hypoglossal and vagus nerves. This variation is termed "vagohypoglossal superior root" and previous case reports described both nerves as being of uniformed thickness [5, 8]. In Type IV variation, the superior root of the ansa cervicalis branches solely off the vagus nerve. Type V variation has C1 fibers going through both the hypoglossal and vagus nerves but no ansa formation.

All of these types, except for Type II, occur in less than 1% of the population [3]. In a typical anatomic presentation, the vagus nerve and hypoglossal nerve exit the skull separately via the jugular foramen and the hypoglossal canal, respectively [11]. However, in this case, the right hypoglossal and vagus nerves were fused immediately after their exit from the hypoglossal and jugular foramina, respectively. The hypoglossal and vagus nerves have an approximately 1.5 cm fused portion, and the superior root of the ansa cervicalis branched solely off the vagus nerve 3 cm from the point of its separation. According to Jelev's classification of known variation in the formation of the ansa cervicalis, this would most closely relate to a Type IV variation. The classic Type IV variation occurs in less than 1% of the population and is described as the superior root of the ansa cervicalis branching solely off the cervical part of the vagus nerve [3, 15]. This case presentation is not a true type IV since the C1 fibers ran along the fused vagal-hypoglossal trunk before the superior root emerged as a vagal ansa [9]. There have been several documented cases of vagal contribution to the superior branch of the ansa cervicalis [3, 5, 8, 15]; however, there has only been one additional case reported of fusion of the hypoglossal and vagus nerves with the ansa cervicalis branching solely off the vagus nerve [11]. While variations of the superior root of the ansa cervicalis are rare, anatomic variations of the inferior root are much more common due

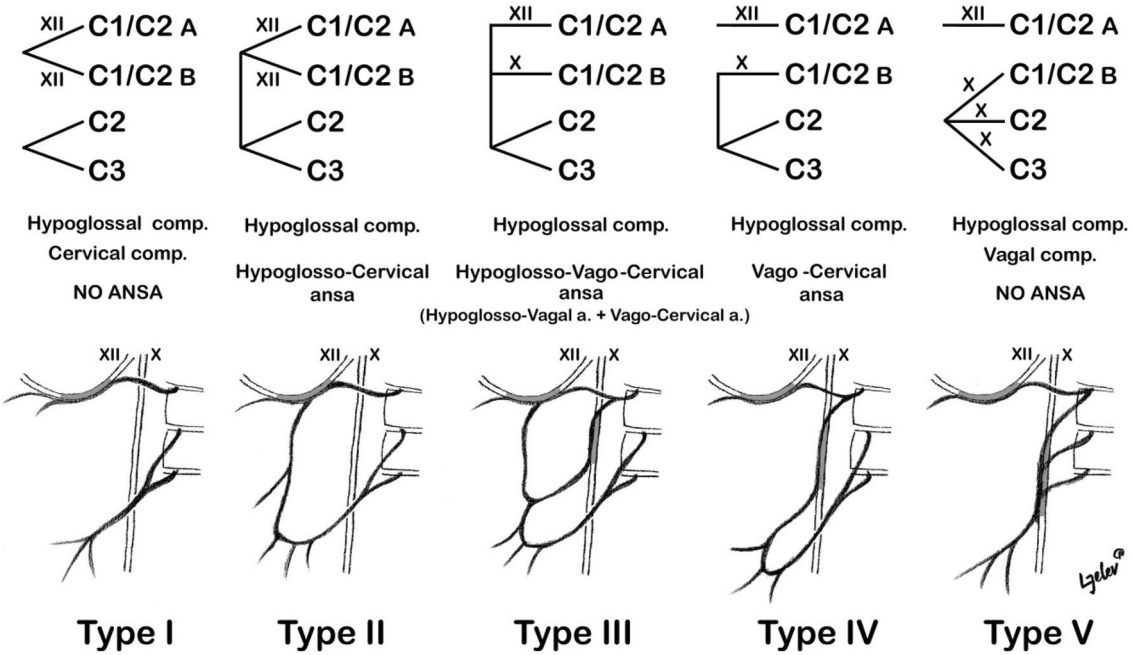

Fig. 3 Common scheme of the proposed classification of the ansa cervicalis in human [3]. (Reprinted by permission from John Wiley and Sons, Clinical Anatomy, *Some unusual types of formation of the ansa cervicalis in humans and proposal of a new morphological classification.* Jelev L, 2013)

to various cervical root contributions that are possible [6, 15]. Bilateral inferior root variations have been documented, whereas there have been no documented cases of bilateral superior root variations [6].

Embryological perspective

The hypoglossal nerve passes through the hypoglossal foramen and emerges out of the skull anterior to the occipital condyle, just anteromedial to the jugular foramen. Embryological evolution has shown that the hypoglossal canal is formed by the fusion of the intervertebral foramina of the area vertebralis of the occipital region [4]. In adults, the canal is separated from the jugular opening by the jugular tubercle, which is highly variable in shape and size [14]. In this case, it was likely that the tubercle was narrow, and the external opening of the hypoglossal canal was in close proximity to the jugular opening.

The hypoglossal nerve is a purely somatic motor nerve formed from the union of several pre-cervical nerves that innervate the occipital myotomes, which develop into the tongue muscles [12]. C1-3 nerves are ventral rami and supply the supra and infrahyoid muscles that developed from the cervical somites. Hence, the hypoglossal nerve is in close proximity to the upper cervical nerves, which is the likely reason for the C1 root coursing along the hypoglossal nerve for a short distance before separating as ansa hypoglossi or the superior root of ansa cervicalis. Besides the motor fibers, communication between the cervical and hypoglossal nerves carries afferent fibers from the meninges [5].

The vagus nerve is a mixed nerve with extensive sensory and motor functional components [12]. In an embryo, several communications exist between the nodose ganglion of the vagus and the hypoglossal nerve [12]. In adults, communications between the vagus nerve and the hypoglossal nerve containing an intermixture of afferent and efferent fibers of the tongue have been shown [12]. Besides these fibers, the functional components of the vagus nerve are distinct from the hypoglossal nerve [12]. The extensive communication at the nodose ganglion and proximity of the two nerves likely caused the fusion of the vagus and hypoglossal trunk in this case.

An extension of C1 fibers into the vagus nerve results in a vago-cervical complex [14]. Since the vagus and hypoglossal nerves were fused, the C1 fibers most likely formed a vago-cervical complex and traveled along the fused hypoglossal-vagus trunk before entering the hypoglossal nerve (to supply geniohyoid and thyrohyoid) while some fibers continued in the vagus nerve before separating as the superior root of ansa cervicalis (to supply the infrahyoid muscles). It was likely that the vagus nerve, hypoglossal nerve, and C1 fibers had pseudo communications with no fiber exchange but were attached by connective tissue fibers only.

Ansa cervicalis implications

Typical innervation of the sternohyoid, sternothyroid, and superior belly of the omohyoid occurs through the superior root of the ansa cervicalis branching off the hypoglossal nerve [5, 9]. However, this case displays unusual participation of the vagus nerve in the innervation of these muscles by the superior root branching off the vagus nerve [9]. Due to this arrangement, paralysis of the infrahyoid muscles may occur following a lesion of the vagus nerve anywhere in the neck proximal to the branching point of the vagal ansa [5, 16]. This variation in the anatomy of the ansa cervicalis could be of considerable clinical significance to surgeons, as the infrahyoid muscles have important roles in deglutination and phonation, so any abnormality in innervation could cause confusion [3, 9, 11]. This is particularly important for surgeons who perform reinnervations of laryngeal and facial muscles, as the ansa cervicalis is the prime choice due to its proximity to the recurrent laryngeal nerve and its involvement in phonation [3, 9, 11]. Surgeons prefer to use the ansa cervicalis, instead of the hypoglossal nerve, to reanimate the face following facial nerve palsy to eliminate potential future complications with phonation and deglutition from hypoglossal nerve deterioration [9]. Although there has been debate over which branch of the ansa cervicalis should be used in these procedures, the use of the superior root has been reported to improve surgical outcomes [5]. The point of separation of the vagus from the hypoglossal may be confused for the superior root coming off the hypoglossal, and the vagus may be inadvertently used as the nerve graft; this may result in severe complications [16]. Knowledge of ansa cervicalis anatomic variations could help to prevent iatrogenic vagus nerve injuries during harvesting procedures [16].

Hypoglossal neurofibroma

Peripheral nerve sheath tumors (PNST's) are a subset of neuroepithelial tumors affecting the cells comprising the myelinated nerve covering. Most PNSTs are benign in nature and are classified as neurofibromas or Schwannomas [1]. Literature suggests that only 5% of the neurogenic tumors in the neck arise from the hypoglossal nerve [7]. Hypoglossal neurofibromas are rare, slow-growing, benign neoplasms of the peripheral nerve sheath consisting of Schwann cells, perineurial cells, collagen fibers, and fibroblasts that are relatively circumscribed but unencapsulated [1]. Schwannomas differ from neurofibromas in that they consist only of Schwann cells and are fully encapsulated [10]. PNST's of the hypoglossal nerve are classified into the following three subtypes: intracranial (Type A), intracranial-extracranial (Type B), and extracranial (Type C) [10], with the vast majority occurring intracranially

[1]. It is estimated that around 30% of hypoglossal tumors extend extracranially. However, purely extracranial hypoglossal neurofibroma is exceedingly rare and has only been reported in two cases. [1, 2].

Most of these neurofibromas occur sporadically, with 10% of cases associated with Neurofibromatosis type 1 (NF-1) [1, 7]. NF-1, an autosomal dominant disorder caused by a somatic mutation in the NF-1 gene, affects roughly 1 in 2500 births and is characterized by diffuse neurofibromas, café-au-lait spots, and optic disturbances [7]. Neurofibromas in the cervical region most frequently occur in the cervical plexus, brachial plexus, and vagus nerve [1]. Of the few reported cases of hypoglossal neurofibromas, there are only two case reports of hypoglossal neurofibromas occurring in the cervical region [1, 2]. One of these cases indicated that the patient had NF-1 [7]. Due to donor privacy regulations and ethical concerns, researchers were not able to conduct genetic testing to officially exclude neurofibromatosis as a diagnosis; however, no additional tumors nor any other visible signs of disease (café-au-lait spots, Lisch nodules, etc.) were noted during dissection.

Hypoglossal neurofibroma implications

Although neurofibromas are often benign and asymptomatic, they can present with dysphagia, dysphonia, tongue wasting on the affected side and other symptoms depending on the size, location, and vascularity of the tumor [10, 11, 13]. While MRI is the preferred diagnostic modality for PNSTs, surgeons often utilize additional forms of imaging, such as high-resolution MR neurography, to anatomically map the tumor and adjacent nervous and vascular structures to assist with preoperative planning [10, 13]. Fine needle aspiration and biopsies can also be performed to distinguish among PNSTs, but the former only has a 60% likelihood of providing an accurate interpretation of results, while the latter is not recommended due to excessive bleeding and scarring around the tumor [13]. Resection of a hypoglossal neurofibroma carries a risk of neural dysfunction, as neurofibromas usually involve fascicles of the original nerve that are indistinguishable from surrounding nerve tissue, thereby making complete resections difficult without sacrificing portions of the parent nerve [7]. Despite this, microsurgical resections are still the preferred method of treatment because neurofibromas are relatively radio and chemo-resistant [7, 10, 13]. Due to the high rate of morbidity associated with complete microsurgical resections, subtotal and near-total resections are sometimes offered as an alternative approach [13]. However, recent advancements in microsurgical techniques have significantly decreased postoperative complications and reported mortality rates to as low as 1% [13].

Conclusion

The anatomical variations of ansa cervicalis, coexistent vagus-hypoglossal nerve fusion, and rare location of the extracranial hypoglossal tumor represent an exceptionally unique case presentation. Despite known cadaveric research limitations, this study documents and furthers the knowledge of these coexistent findings and contributes to the currently limited body of related clinical and anatomical research. Although donor privacy regulations prevented researchers from excluding neurofibromatosis as a differential diagnosis, researchers are confident this condition did not clinically contribute, considering no other tumors were found during thorough dissection. Additionally, the clinical implications of a variant ansa cervicalis should be considered, particularly among otolaryngology surgeons. Knowledge of ansa cervicalis anatomical variations and localization of structures is vital for maximizing otolaryngological surgical outcomes. In a clinical setting, a combination of patient history, genetic testing, the radiographic and histopathological examination could be utilized for diagnostics and various surgical interventions. This case may benefit from future research to better understand the pathogenesis and clinical significance of the findings.

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Declarations

Conflict of interest The authors have no competing interests to declare that are relevant to the content of this article.

Ethical approval Since the research was on a cadaver, the Marian University Institutional Review Board cleared and indicated that the study did not need a review or approval (IRB#B22.101).

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