Neurovascular compression syndrome: Trigeminal neuralgia, hemifacial spasm, vestibular paroxysmia, glossopharyngeal neuralgia, four case reports and review of literature

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ABSTRACT
Neurovascular compression syndrome is caused by vessels touching a cranial nerve, resulting in clinical manifestations of abnormal sensory or motor symptoms. The most common manifestations are trigeminal neuralgia and hemifacial spasm. However, neurovascular compression of the vestibular nerve or glossopharyngeal nerve are rare. In this article, we describe four typical cases of neurovascular compression syndrome. In addition, we analyze the main features of the etiology, neuroimaging, and treatment of this disease.

1. Introduction
Neurovascular compression syndrome (NVCS) is a condition due to compression of the cranial nerve by adjacent vessels[1]. The most common manifestations are trigeminal neuralgias (TN), hemifacial spasm (HFS), however, reports of vestibular paroxysmia (VP) and glossopharyngeal neuralgia (GPN) are rare. Moreover, reviews and analyses of the pathology, symptomatology, neuroimaging, and treatment of NVCS are lacking. Here, we present four typical cases of NVCS and provide a literature review of previously reported cases to guide clinical practice.

2. Case description

2.1. Case 1
A 37-year-old man presented to our neurology department with involuntary contractions of his left face for 1 year. The patient stated that the contractions in his face can be triggered during nervousness. He used to be in good health. Neurologic examination revealed no obvious signs other than the involuntary facial contractions. Magnetic resonance angiography (MRA) of the brain revealed that the left vertebral artery was compressing the left facial nerve, facial spasm (left side) caused by NVCS was diagnosed (Fig. 1). After injection of botulinum toxin, the symptoms improved significantly.

2.2. Case 2
A 65-year-old man was referred to our neurology department complaining of recurrent paroxysmal pain on the right-sided of his face for one week. Each episode occurred during speech, which is transient but severe. In addition, the symptom was already interfering with sleep. According to the ICHD-3 diagnostic criteria for classic TN from the International Classification of Headache Disorders, the patient was diagnosed with trigeminal neuralgia (right) caused by NVCS with its typical clinical symptoms and brain MRI (Fig. 2). After radiofrequency ablation of the trigeminal nerve, no further episodes of facial pain occurred.

2.3. Case 3
A 47-year-old man with a 1-week history of severe pharyngeal pain after swallowing. He had no history of other diseases except for type 2 diabetes. No other signs were noted on neurologic examination. Magnetic resonance imaging (MRI) of the brain revealed that the tortuous left aorta was compressing the glossopharyngeal nerve (Fig. 3). According to ICHD 3 diagnostic criteria, glossopharyngeal neuralgia caused by NVCS was diagnosed. After decompression of the glossopharyngeal nerve, there was improvement of symptoms.

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2.4. Case 4

A 51-year-old man patient visited our neurology department because he had been suffering from paroxysmal vertigo during walking for 3 days, with each attack lasting only seconds, without nausea, vomiting, or loss of consciousness. His medical history was unremarkable. No other signs were noted on neurologic examination. Vestibular paroxysm due to NVCS was diagnosed after an MRI scan of the brain, which revealed that the left anterior cerebellar artery was compressing the vestibular nerve (Fig. 4). Carbamazepine (0.1 g bid) was recommended, and improvement in the patient’s symptoms was observed after 3 days.

3. Discussion and literature review

3.1. Clinical symptoms of NVCS

Trigeminal neuralgia (TN), which affects 4–13 people per 100,000 each year, is characterized by transient and episodic, electric shock-like or stabbing, recurrent episodes of unilateral pain occurring in one or more segments of the trigeminal nerve and triggered by innocuous stimuli such as touch, chewing, or speaking [2]. The clinical feature is the basis of TN diagnosis [3]. TN and hemifacial spasm (HFS) are the most common clinical manifestations of NVCS. Vestibular paroxysmal (VP) and glossopharyngeal neuralgia (GPN) are other manifestations of NVCS. In addition, there is extremely rare compression of cranial nerves such as the oculomotor nerve or vagus nerve by vessels. Patients with
NVCS may experience impaired quality of life, significant psychosocial impairment, depression, and even suicidality before appropriate treatment is given [4]. Therefore, it is very important for physicians to diagnose and treat NVSC to improve patients’ symptoms as early as possible.

HFS is defined as unconscious, uncontrollable, intermittent involuntary twitching of muscles innervated by the ipsilateral facial nerves and classically begins unilaterally in the upper face [5,6]. Brief, repetitive twitches cause sudden and involuntary closure of the eyes and then extend to the cheeks, mouth, and lower neck [7,8]. Other manifestations in patients with HFS include paroxysmal ringing in the ears due to involvement of the stapedius muscle, unilateral or bilateral hearing loss, or mild facial nerve palsy, and stress or anxiety may exacerbate HFS, while relaxation may relieve symptoms [9]. Women are more at risk than men [10]. It rarely occurs bilaterally. Even in bilateral cases, it develops unilaterally and affects the other side after months to years [8]. When the trigeminal nerve is affected simultaneously, it is called convulsive tic [11].

The symptoms of vestibular paroxysmia (VP) are periodic, spontaneous, brief rotating or non-rotating vertigo attacks accompanied by postural and gait unsteadiness, with or without tinnitus, hearing loss, or hyperacusis. Tinnitus usually lasts less than 1 min and occurs 30 or more times per day [12]. VP is often triggered by certain head positions, hyperventilation, or changes in head posture [13]. The incidence of VP is not yet known [14]. In a group of more than 17,000 patients in tertiary care centers with dizziness and vertigo, the relative frequency of VP was about 4% [14].

Glossopharyngeal neuralgia (GPN) is a severe, transient, stabbing, unilateral pain in the ear, base of the tongue, tonsillar fossa, and/or below the angle of the jaw [2]. The incidence of GPN is approximately 0.8 per 100,000 population per year [15]. The pain occurs in the area of the extensions of the glossopharyngeal nerve [16]. It is often triggered by coughing, speaking, swallowing, or yawning. They occur in paroxysmal attacks lasting from a few seconds to 2 min. In about 10% of GPN patients, the pain attacks are associated with vagal symptoms such as cough, hoarseness, bradycardia, hypotension, syncope, seizures, or even cardiac arrest [17]. In rare cases, GPN may manifest as syncope without pain, making a definitive diagnosis very difficult [18].

3.2. Etiology and imaging of NVCS

Classic TN (80–90%) is caused by compression of the trigeminal root by adjacent vessels [19], resulting in flexion, torsion, furrowing, demyelination, and atrophy of the trigeminal nerve [20]. The main causative vessel of TN is the superior cerebellar artery (SCA) [10]. TN is most common compared to the other three manifestations of NVCS, perhaps because the trigeminal nerve has the longest and most voluminous central myelin portion among the cranial nerves, providing a larger area for vascular compression [21]. The demyelination hypothesis is one of the main causes of the pathogenesis and pathophysiologic of TN [22]. However, demyelination blocks impulse propagation, resulting in local numbness instead of paroxysmal pain [23]. Simple demyelination does not directly explain the characteristic symptoms of the disease: paroxysmal pain. Therefore, the inflammatory hypothesis is proposed to provide a rational explanation for paroxysmal pain [23]. According to the bioresonance hypothesis, it is known that the fibers of the trigeminal nerve are destroyed when the vibration frequency of the trigeminal nerve is close to the surrounding structures, resulting in abnormal transmission of impulses and causing facial pain [24]. Increasing evidence suggests that voltage-gated sodium channels (VGSCs) also play an important role in the development of trigeminal afferents [25,26]. Some studies using the TN model of infraorbital nerve constriction have shown that VGSCs can regulate TN pain [27].

Since 1951, there has been controversy between two hypotheses regarding the pathophysiological mechanism of HFS [28]. The core/central hypothesis assumes that facial nerve injury may lead to degenerative medullary changes in the functional junction of the facial nerve core, and that the formation of dendritic spines may cause excessive excitation of the core. The peripheral hypothesis suggests that clinical symptoms are caused by ectopic impulse generation at the lesion site and interaction between fibers. However, these hypotheses lack data on abnormal muscle response (AMR) [11]. AMR is a particular facial electromyographic phenomenon in patients with HFS. When one branch of the facial nerve is stimulated, the myoelectric response can be recorded on muscles innervated by other branches, but it can only be detected on the affected side [29]. There is another hypothesis, the sympathetic hypothesis, which states that the ectopic action potential of the facial nerve is triggered by sympathetic nerves in the adventitia of the causative artery [30]. Currently, the main cause of HFS is thought to be the facial nerve REZ compressed by the arterial loop, usually the posterior inferior cerebellar artery/anterior inferior cerebellar artery (PICA/AICA), tumor, cyst, or aneurysm [31]. It has been suggested that repeated compression of the facial nerve by the vascular loops leads to mild but significant demyelination, resulting in muscle weakness. The longer HFS persists, the more severe the spasms and muscle weakness [32].

A neurovascular conflict of the eighth cranial nerve is the reason for the transient vertigo of VP [33]. Symptoms are usually caused by direct pulsatile compression accompanied by brief discharges, and vertigo accompanied by paroxysmal pulsatile tinnitus is more likely to be associated with vascular compression [4]. Deformed, elongated, and dilated cerebellopontine arteries are thought to be the cause of segmental and compressive nerve injury accompanied by demyelination. The AICA is the most common vessel responsible for this [13].

Idiopathic GPN may be caused by severe demyelination and axonal degeneration of cranial nerve fibers IX and X [17]. The most common causative vessel is the posterior inferior cerebellar artery (PICA) and/or AICA [34].

However, there is no hypothesis for VP and GPN. These four manifestations of NVCS share a similar etiology: demyelination and mechanical stimulation by neurovascular conflict. Neuroimaging such as magnetic resonance imaging (MRI), high-resolution brain MRI (HRMRI), and magnetic resonance angiography (MRA) can help visualize the cause of structural disease and the etiology of vascular compression [19]. Fusion MR imaging combining steady-state MRI and three-dimensional time-of-flight MR angiography (3D-TOF-MRA) can observe cranial nerve REZ and exclude the presence of tumors, arachnoid cysts, giant carotid basilar artery, lacunar infarction, or brainstem plaques in the pons and cerebellar angle [12]. A prospective, double-blind, controlled study suggests that diffusion tensor imaging (DTI) parameters can reveal focal demyelination and trigeminal nerve (TGN) damage, and DTI could potentially identify atrophy of the TGN in TN [35]. Electroneuromyography (ENMG) to characterize the nature of nerve excitability disorder [8]. Color duplex ultrasound can be used to identify hemodynamic changes in the PICA and AICA on the HFS side [36]. Balloon test occlusion can contribute to the definitive diagnosis of atypical GPN patients [37].

3.3. Management of NVCS

3.3.1. Oral medication

Anticonvulsants such as carbamazepine and oxcarbazepine are effective drugs of choice for the treatment of classic TN, idiopathic TN, VP, or GPN [19,38,39]. The mechanism is to regulate VGSCs, resulting in decreased neuronal activity. Possible side effects of carbamazepine include drowsiness, dizziness, diplopia, or nausea. Oxcarbazepine is a relatively new drug that is increasingly used as a first-line treatment for patients who do not respond to or cannot tolerate carbamazepine. Recently, many researchers are exploring new pharmacological alternatives, such as the active metabolite of oxcarbazepine and the new Nav1.7 blocker vixotrigine [10,40]. It has been confirmed that topiramate can also significantly improve the quality of life of VP patients.
33% had desired outcomes (no pain, no medication needed) [55]. Patients who were followed up for at least 36 months, 50% had good outcomes and about one-third had a lasting favorable response. R.I. Riesenburger et al. found that in a series of TN patients who received a single GKS treatment and were disease-free at one year, 61% had long-term success [54]. This suggests that GKS can be an effective treatment for TN [54].

3.3.2. Botulinum toxin injection

Botulinum toxin (BTX) injection is the first-line treatment for HFS [6]. BTX can be injected subcutaneously or intramuscularly into the affected facial muscles, is less invasive, and is easily accessible to physicians [44]. Injection of BTX is also beneficial, especially for middle-aged and elderly patients with TN who do not respond to medication or cannot tolerate side effects [45]. These complications usually resolve within a few days to weeks. The weakness of BTX injection is that repeated injections have a high economic cost and provide only symptom relief.

3.3.3. Microvascular decompression

Microvascular decompression (MVD), a surgical procedure aimed at separating the causative vessel from the compressed nerve, is an effective treatment with a high success rate for relieving symptoms caused by NVCS [46]. It is the most effective method for treating TN, HFS, VP or GPN when oral medications or BTX injections have failed to provide benefit [6,12,44,47]. In about three-quarters of patients with pharmacoresistant TN, the symptom disappears after MVD. Shorter disease course, arterial compression, and Burchiel type 1 classification (classic TN) may indicate more favorable outcomes [48]. A retrospective study has shown that older patients can undergo MVD compared to younger patients with careful evaluation. From a technical point of view, MVD in elderly patients is favored by the relative atrophy of the brain, which reduces the need for cerebellar retraction and facilitates surgical access. Therefore, age should not be considered a contraindication to MVD [49].

It is worth mentioning that intraoperative monitoring of AMR facial nerve electromyography can improve the safety of surgery and the prognosis of MVD [50]. Monitoring lateral spread response (LSR) during surgery is helpful for the surgeon to identify the culprit vessel, and persistence of LSR increases the incidence of HFS recurrence after MVD [51]. Saleem I. Abdulrauf et al. supported that awake intraoperative peripheral nerve stimulation occurs, such as hemifacial spasm, trigeminal neuralgia, glossopharyngeal neuralgia, and paroxysmal vestibular syndrome, etc., the etiology of neurovascular compression should be considered. TOF-MRA and HRMRI can be used as useful diagnostic imaging modalities. MVD is an effective treatment for NVCS.

4. Conclusion

The clinical manifestations of NVCS are complex. When symptoms of cranial nerve stimulation occur, such as hemifacial spasm, trigeminal neuralgia, glossopharyngeal neuralgia, and paroxysmal vestibular syndrome, etc., the etiology of neurovascular compression should be considered. TOF-MRA and HRMRI can be used as useful diagnostic imaging modalities. MVD is an effective treatment for NVCS.

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4.2. Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

4.3. Ethics statement

Written informed consent was obtained from the patient for the publication of this case report, including any potentially identifiable images or data included in this article.

Author contributions

XZX and XL were involved in the work-up of the patient, planning and conducting investigations, and providing clinical care. XL planned the case report and modified the manuscript. SXH and ZXR contributed to collecting the relevant literature and drafted the initial manuscript. All authors read and approved the final version of the manuscript.

References

[1] S. Haller, L. Etienne, E. Kövari, A.D. Varoquaux, H. Urbach, M. Becker, Imaging of neurovascular compression syndromes: trigeminal neuralgia, hemifacial spasm, vestibular paroxysmia, and glossopharyngeal neuralgia, Am. J. Neuroradiol. 37 (2016) 1384-1392, https://doi.org/10.3174/ajnr.A4683.
[2] The International Classification of Headache Disorders, 3rd edition (beta version), Cephalalgia 33 (2013) 629-808, https://doi.org/10.1177/0333102413485668.
[3] K.W. Al-Quliti, Update on neurosurgical pain treatment for trigeminal neuralgia, Pharmacol. Surg. Options, Neurosci. (Riyadh) 20 (2015) 107–114, https://doi.org/10.17172/ins.2015.2.20140501.
[4] T.-P. Chang, Y.-C. Wu, Y.-C. Hsu, Vestibular paroxysmia associated with paroxysmal palatal tinnitus: a case report and review of the literature, Acta Neurol. Taiwan 22 (2013) 72-75.
[5] N. Chaudhry, A. Srivastava, L. Joshi, Hemifacial spasm: the past, present and future, J. Neurol. Sci. 356 (2015) 27-31, https://doi.org/10.1016/j.jns.2015.06.032.
[6] T.R. Chopade, P.C. Bolli, Hemifacial Spasm, in: StatPearls Publishing, Treasure Island (FL), 2022. http://www.ncbi.nlm.nih.gov/books/NBK526180/ (accessed June 23, 2022).
[7] A.C. Felício, C. de O. Godeiro-Junior, V. Borges, S.M. de A. Silva, H.B. Ferraz, Bilateral hemifacial spasm: a series of 10 patients with literature review, Park. Relat. Disord. 14 (2008) 154-156, https://doi.org/10.1016/j. parkreldis.2007.06.001.
[8] J.-P. Lefaucheur, N. Ben Daamer, S. Sangla, C. Le Guerin, Diagnosis of primary hemifacial spasm, Neurochirurgie 64 (2018) 82-86, https://doi.org/10.1016/j.neuchi.2017.12.003.
[9] L. Wang, X. Hu, H. Dong, W. Wang, Y. Huang, L. Jin, Y. Luo, W. Zhang, Y. Lian, Z. Liang, H. Shang, Y. Feng, Y. Wu, J. Chen, W. Luo, X. Wan, Clinical features and treatment status of hemifacial spasm in China, Chin. Med. J. 127 (2014) 845-849.
[10] S.K.N., N. S, Trigeminal Neuralgia, PubMed, 2021. https://pubmed.ncbi.nlm.nih.gov/32119073/ (accessed February 24, 2021).
[11] A.Y. Lu, J.T. Yeung, J.L. Gerrard, E.M. Michaelides, R.F. Sekula, K.R. Bulsara, Hemifacial Spasm and Neurovascular Compression, ScientificWorldJournal (2014) (2014), https://doi.org/10.1155/2014/3493919.
[12] T. Brandt, M. Strupp, M. Dieterich, Vestibular paroxysmia: a treatable neurovascular cross-compression syndrome, J. Neurol. 263 (Suppl 1) (2016) S90-S96, https://doi.org/10.1007/s00415-015-7973-3.
[13] K. Hüther, D. Barresi, M. Glaeser, J. Linn, C. Adrian, U. Mansmann, T. Brandt, M. Strupp, Vestibular paroxysmia: diagnostic features and medical treatment,
