

## NEUROVASCULAR COMPRESSION SYNDROME IN TRIGEMINAL NEURALGIA

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NEUROVASCULAR COMPRESSION SYNDROME IN TRIGEMINAL NEURALGIA (abstract) :  
The trigeminal neuralgia due to neurovascular conflict is a neurosurgical pathology which requires a preoperative accurate imagistic identification. Therefore, neuroimaging studies and detailed knowledge of the cerebellopontine angle anatomy and posterior fossa is imperious for the surgeon. Preoperative acknowledgement of the neurovascular compression of trigeminal nerve is useful both for a right surgical indication and for excluding other causes of trigeminal neuralgia. **Key-words :** TRIGEMINAL NEURALGIA, NEUROVASCULAR COMPRESSION SYNDROME, TRIGEMINAL NERVE

“As we age, our arteries elongate and our brains sag” (1).

Peter J. Jannetta (1932-2016)

### INTRODUCTION

The most frequent cause of trigeminal neuralgia (TN) is the focal compression of the nerve V (n.V) at the entry into pons, also called root entry zone, most of the time, produced by an artery or a vein (2). In this respect, literature reports that 80-90% of the cases of TN are related to artery or vein compression of the trigeminal nerve root (2, 3).

Although the pathophysiology of TN is not fully understood, post-surgical histopathological studies of neurovascular compression syndrome (NVCS) revealed several pathological mechanisms which take place at the root of the trigeminal nerve and which try to explain the symptomatology.

This paperwork intends to be a review of NVCS in TN, by aiming at understanding this

syndrome and the main pathological mechanisms involved in the NVCS of n.V.

### NEUROVASCULAR COMPRESSION SYNDROME

N.V is the largest cranial nerve and has both a sensitive and motor composition, since it is the main nerve of the first brachial arch (4). Due to its extensive distribution in the head and supra hyoid neck, its branches can be involved in a multitude of disease entities (5, 6).

Cranial nerves are surrounded by a myelin sheath, which provides protection and metabolic support for the axon. Oligodendrocytes form the myelin in the central nervous system, while Schwann cells form the myelin in the peripheral nervous system (7). Between these two types of myelin (central and peripheral

myelin), there is a transition zone (TZ), which is more vulnerable to motor injury and also involved in the emergence of NVCS (8, 9).

This TZ of the nerve is defined as the region which extends from nerve's point of entry into or exit from brainstem to the point of transition from the central myelin (derived from the oligodendroglia) to the peripheral myelin (derived from Schwann cells) (2, 10).

The 3 main branches of n.V (the ophthalmic division V1, the maxillary division V2 and the mandibular division V3) are responsible for sensory innervation of the face and, by the Gasserian ganglion, they send a sensory input to the brainstem via the cisternal portion. This cisternal portion of n.V has a length comprised between 8 and 15 mm and the zone with central myelin (distance from brainstem to TZ) is shorter on the medial side of the nerve (1.13 mm) than on its lateral side (2.47 mm) (9). This TZ is different among the cranial nerves, so that nerve VIII has the longest transition zone compared to cranial nerves V, VII or IX (11).

#### PHYSIOPATHOLOGY OF THE NEUROVASCULAR CONFLICT

Despite the fact that the pathophysiology of TN is not fully understood, post-surgical histopathological studies of NVCS revealed several physiopathological mechanisms in the TN, out of which the most important are: (1) *demyelination*, (2) *focal axonal degeneration* (12, 13, 14, 15), (3) *loss of axons* (15) and (4) *abnormal re-myelination* (2). The most important and commonly found in 90% of the cases is demyelination of the sensory fibers of the n.V (14). This demyelination of the nerve causes an aberrant impulse generation which explains the clinical manifestations of NVCS, as well as the severe pain (16).

The first research on early ultrastructural modifications of n.V in NVCS were carried out in the 60s-70s and used to describe only a few anomalies: proliferative degenerative changes and myelin disintegration (17, 18). Twenty years later, Hilton and his collaborators published a study on focal loss of myelin, close apposition of demyelinated axons, along with a few residual oligodendrocytes without inflammatory cells (13). Subsequent studies showed that an underlying mechanism involved in NVCS is chronic demyelination, right beneath the region of indentation. Adjacent to this region, thinly

myelinated axons, signs of demyelination and aberrant re-myelination or partial demyelination of the affected nervous fibers were noticed (2, 14, 19).

Love *et al.* observed, in one of his studies, that in light microscopy, the demyelinated axons and the axons with abnormally thin myelin sheath have a caliber similar to normal white matter away from the demyelination (14). As opposed, Devor *et al.*, found out that the massive injury of nerve fibers of n.V is directly proportional to the degree of compression noted by the neurosurgeon during the operation (15).

#### PREDISPOSING CONDITIONS

There is a series of anatomic conditions which may predispose to NVCS: a small-dimension posterior fossa (12), crowded or angled cerebellopontine cistern, (20), angulation of the nerve crossing over de petrous ridge, arachnoid adhesions (12), skull base deformities, like platybasia (21) or tentorium agenesis which, by the herniation of the temporary lobe into posterior fossa, brings about the reduction of ipsilateral cerebellopontine angle cistern along with the exacerbation of neurovascular conflict (22).

To these anatomical conditions, acquired factors are added, such as: hypertension and aging, which accelerate the emergence of atherosclerosis that leads to blood vessels ectasia and emergence of vascular compression (23). Since the 1980s, when the American neurosurgeon Peter J. Jannetta (1932-2016), who developed and innovated procedures of microvascular decompression of n.V, emphasized the effect of cerebral vessels' aging in the emergence of this neurovascular conflict. Pioneering neurosurgeon on microvascular decompression and facial pain, Jannetta argued that besides atherosclerotic or redundant arterial loops, also the intrinsic and bridging veins of brainstem or cerebellum can cause the cross-compression of the cranial nerves in the cerebellopontine angle with secondary dysfunction of them (1, 2).

#### STRUCTURES WHICH CAN COMPRESS THE TRIGEMINAL NERVE

Vascular compression of n.V can be localized anywhere in the n.V trajectory: juxtaponine, midcisternal or juxtapetrous (24, 25) and most of the time, it is produced by the arteries, veins, aneurisms or arteriovenous malformations.

**Arteries.** Although any structure in the posterior fossa can compress n.V, the most commonly found are arteries. This can be explained by a bigger pressure in the arteries and consecutive pulsatility (25, 26), while acquired atherosclerosis in these arteries may lead to their ectasia. The most commonly found arteries in the n.V. compression are : superior cerebellar artery (SCA) and anterior inferior cerebellar artery (AICA) (27). Hence, 60-90% of the NVCS cases involve the SCA (2, 28, 29) while <25%, involve the AICA (12).

Normally, SCA is localized medial to the nerve root, with a descending proximal portion then a loop and an ascending distal portion. (24). The loop size is variable and better represented in patients with NVCS. As for the AICA, this also presents a proximal ascending portion, then a loop and a descending distal portion. Usually, in NVCS, the neurovascular conflict takes place in this loop (24).

Other arteries which may compress n.V are : vertebral and basilar arteries (30, 31), posterior inferior cerebellar artery (PICA) (32), labyrinthine arteries (32) but also carotid-basilar anastomosis persistence, especially a persistent trigeminal artery (33, 34, 35).

**Veins.** Other vascular structures which may compress n.V are veins, usually associated with an arterial conflict (approximately 27%) and seldom, by themselves (7%) (12, 36). Normal vein anatomy in this region is variable and the most important vein involved in NVCS are :

the vein of the medial cerebellar peduncle, superior petrous vein and the cerebellar-pontine scissure vein. These can compress the n.V either perpendicularly or parallel to the nerve root (24).

In the Meckel's cave, n.V can also be compressed by the transverse pontine vein (37). Other veins which may cause a neurovascular conflict of n.V are : pontotrigeminal, cerebellopontine fissure, lateral mesencephalic and middle cerebellar peduncle veins (32) or petrosal sinus secondary to a carotid-cavernous fistula (38).

**Arteriovenous malformations and aneurysms.** Arteriovenous malformations and arteriovenous fistula of the posterior fossa can produce TN through vessels which may compress n.V. (39, 40, 41, 42, 43, 44). Also, venous angioma (45) dural fistulas, aneurysms of the internal carotid artery, posterior communicating artery, AICA or SCA (46, 47) can compress n.V.

## CONCLUSIONS

TN caused by neurovascular compression of n.V. is a neurosurgical pathology which, besides the preoperative neuroimaging identification, requires very detailed knowledge about the cerebellopontine angle anatomy and posterior fossa. Therefore, preoperative imaging studies are useful not only in accurately identifying the neurovascular compression, but also in providing a correct indication of the surgery and excluding other causes of TN.

## REFERENCES

1. Jannetta PJ. Neurovascular compression in cranial nerve and systemic disease. *Ann Surg*, 92(4) : 518-525, 1980.
2. Love S, Coakham HB. Trigeminal neuralgia : pathology and pathogenesis. *Brain*, 124 : 2347-2360, 2001.
3. Hamlyn PJ. Neurovascular relationships in the posterior cranial fossa, with special reference to trigeminal neuralgia. 2. Neurovascular compression of the trigeminal nerve in cadaveric controls and patients with trigeminal neuralgia : quantification and influence of method. *Clin Anat*, 10 : 380-88, 1997.
4. Monkhouse S. The trigeminal nerve, in Monkhouse S (editor) *Cranial nerves functional anatomy*. Cambridge : Cambridge University Press, 2006, p. 50-65.
5. Williams LS, Schmalfuss IM, Sistrom CL, *et al.* MR imaging of the trigeminal ganglion, nerve, and the perineural vascular plexus : normal appearance and variants with correlation to cadaver specimens. *AJNR Am J Neuroradiol*, 24 : 1317-1323, 2003.
6. Gonella MC, Fischbein NJ, So YT. Disorders of the trigeminal system. *Semin Neurol*, 29 : 36-44, 2009.
7. Haller S, Etienne L, Kövari E, *et. al.* Imaging of neurovascular compression syndromes : trigeminal neuralgia, hemifacial spasm, vestibular paroxysmia, and glossopharyngeal neuralgia, *AJNR Am J Neuroradiol*, 37 : 1384-1392, 2016.
8. Tarlov IM. Structure of the nerve root, I : nature of the junction between the central and the peripheral nervous system. *Arch Neur-Psych*, 37 : 555-583, 1937.

9. Peker S, Kurtkaya O, Uzün I, *et al.* Microanatomy of the central myelin-peripheral myelin transition zone of the trigeminal nerve. *Neurosurgery*, 59 : 354-359, 2006.
10. Lutz J, Linn J, Mehrkens JH, *et al.* Trigeminal neuralgia due to neurovascular compression : high-spatial-resolution diffusion-tensor imaging reveals microstructural neural changes. *Radiology*, 258 : 524-530, 2011.
11. Skinner H. Some histologic features of the cranial nerves. *Arch Neur Psych*, 25 : 356-372, 1931.
12. Sindou M, Leston J, Decullier E, *et al.* Microvascular decompression for primary trigeminal neuralgia : long-term effectiveness and prognostic factors in a series of 362 consecutive patients with clear-cut neurovascular conflicts who underwent pure decompression. *J Neurosurg*, 107 : 1144-1153, 2002.
13. Hilton DA, Love S, Gradidge T, Coakham HB. Pathological findings associated with trigeminal neuralgia caused by vascular compression. *Neurosurgery*, 35(2) : 299-303, 1994.
14. Love S, Hilton DA, Coakham HB. Central demyelination of the Vth nerve root in trigeminal neuralgia associated with vascular compression. *Brain Pathol*, 8 (1) : 1-11, 1998.
15. Devor M, Govrin-Lippmann R, Rappaport ZH . Mechanism of trigeminal neuralgia : an ultrastructural analysis of trigeminal root specimens obtained during microvascular decompression surgery. *J Neurosurg*, 96 (3) : 532-543, 2002.
16. Docampo J, Gonzalez N, Muñoz A, *et al.* Neurovascular study of the trigeminal nerve at 3 t MRI. *Neuroradiol J*, 28(1) : 28-35, 2015.
17. Beaver DL. Electron microscopy of the gasserian ganglion in trigeminal neuralgia. *J Neurosurg*, 26(1) : 138-150, 1967.
18. Kerr FW, Miller RH. The pathology of trigeminal neuralgia. Electron microscopic studies. *Arch Neurol*, 15(3) : 308-319, 1966.
19. Rappaport ZH, Govrin-Lippmann R, Devor M. An electron-microscopic analysis of biopsy samples of the trigeminal root taken during microvascular decompressive surgery. *Stereotact Funct Neurosurg*, 68 : 182-186. 1997.
20. Park SH, Hwang SK, Lee SH, *et al.* Nerve atrophy and a small cerebellopontine angle cistern in patients with trigeminal neuralgia. *J Neurosurg*, 110 : 633-637, 2009.
21. Kanpolat Y, Tatli M, Ugur HC, *et al.* Evaluation of platybasia in patients with idiopathic trigeminal neuralgia, *Surg Neurol*, 67(1) : 78-81, 2007.
22. Tanaka T, Nakazaki H, Hida T, *et al.* Trigeminal neuralgia associated with tentorial agenesis and temporal lobe herniation - case report. *Neurol Med Chir (Tokyo)*, 40(2) : 124-127, 2000.
23. Moller AR. Vascular compression of cranial nerves : II : pathophysiology. *Neurol Res*, 21 : 439-443, 1999.
24. Lorenzoni J, David P, Levivier M. Patterns of neurovascular compression in patients with classic trigeminal neuralgia : A high-resolution MRI-based study. *Eur J Radiol*, 81(8) : 1851-1857, 2012.
25. Sindou M, Howeydi T, Acevedo G. Anatomical observations during microvascular decompression for idiopathic trigeminal neuralgia (with correlations between topography of pain and site of the neurovascular conflict) : prospective study in a series of 579 patients. *Acta Neurochir (Wien)*, 144 : 1-12, 2002.
26. Campos-Benitez M, Kaufmann AM. Neurovascular compression findings in hemifacial spasm. *J Neurosurg*, 109 : 416-420, 2008.
27. Turliuc DM, Dobrovat B, Cucu AI, *et al.* To be or not to be a neurovascular conflict : importance of the preoperative identification of the neurovascular conflict in the trigeminal neuralgia. *Romanian Neurosurgery*, 30 (3) : 334-341, 2016.
28. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia*, 8 : 1-96, 1988.
29. Adamczyk M, Bulski T, Sowińska J, *et al.* Trigeminal nerve : artery contact in people without trigeminal neuralgia-MR study. *Med Sci Monit*, 13 : 38-43, 2007.
30. Becker M, Kohler R, Vargas MI, *et al.* Pathology of the trigeminal nerve. *Neuroimaging Clin N Am*, 18 : 283-307, 2008.
31. Borges A, Casselman J. Imaging the trigeminal nerve. *Eur J Radiol*, 74 : 323-340, 2010.
32. Harsha KJ, Kesavadas C, Chinchure S, *et al.* Imaging of vascular causes of trigeminal neuralgia. *J Neuroradiol*, 39(5) : 281-289, 2012.
33. Peluso JP, van Rooij WJ, Sluzewski M, *et al.* Superior cerebellar artery aneurysms : incidence, clinical presentation and midterm outcome of endovascular treatment. *Neuroradiology*, 49 : 747-751, 2007.
34. Pereira LP, Nepomuceno LA, Coimbra PP, *et al.* Persistent trigeminal artery : angio-tomography and angio-magnetic resonance finding. *Arq Neuropsiquiatr*, 67(3B) : 882-885, 2009.
35. Bernstein K, Teitelbaum GP, Herman B, *et al.* Coil embolization of a trigeminal cavernous fistula. *AJNR Am J Neuroradiol*, 19 : 1953-1954, 1998.

36. Sindou M, Leston J, Howeidy T, *et al.* Micro-vascular decompression for primary trigeminal neuralgia (typical or atypical). Long-term effectiveness on pain ; prospective study with survival analysis in a consecutive series of 362 patients. *Acta Neurochir (Wien)*, 148 : 1235-1245, 2006.
37. Matsushima T, Huynh-Le P, Miyazono M. Trigeminal neuralgia caused by venous compression. *Neurosurgery*, 55(2) : 334-337, 2004.
38. Tash RR, Sze G, Leslie DR. Trigeminal neuralgia : MR imaging features. *Radiology*, 172(3) : 767-770, 1989.
39. Nishizawa Y, Tsuiki K, Miura K, *et al.* Multiple arteriovenous malformations of left parietal lobe and left cerebellar hemisphere with symptomatic trigeminal neuralgia : a case report. *No Shinkei Geka*, 16 : 625-630, 1988.
40. Du R, Binder DK, Halbach V, *et al.* Trigeminal neuralgia in a patient with a dural arteriovenous fistula in Meckel's cave : case report. *Neurosurgery*, 53(1) : 216-221, 2003.
41. Matsushige T, Nakaoka M, Ohta K, *et al.* Tentorial dural arteriovenous malformation manifesting as trigeminal neuralgia treated by stereotactic radiosurgery : a case report. *Surg Neurol*, 66(5) : 519-523, 2006.
42. Simon SD, Yao TL, Rosenbaum BP, *et al.* Resolution of trigeminal neuralgia after palliative embolization of a cerebellopontine angle arteriovenous malformation. *Cen Eur Neurosurg*, 70(3) : 161-163, 2009.
43. Ito M, Sonokawa T, Mishina H, *et al.* Dural arteriovenous malformation manifesting as tic douloureux. *Surg Neurol*, 45(4) : 370-375, 1996.
44. Machet A, Aggour M, Estrade L, *et al.* Trigeminal neuralgia related to arteriovenous malformation of the posterior fossa : three case reports and a review of the literature. *J Neuroradiol*, 39(1) : 64-69, 2012.
45. Samadian M, Bakhtevvari MH, Nosari MA, *et al.* Trigeminal Neuralgia Caused by Venous Angioma : A Case Report and Review of the Literature. *World Neurosurg*, 84(3) : 860-864, 2015.
46. Charalampaki P, Kafadar AM, Grunert P, *et al.* Vascular decompression of trigeminal and facial nerves in the posterior fossa under endoscope-assisted keyhole conditions. *Skull Base*, 18(2) : 117-128, 2008.
47. Ildan F, Göçer AI, Bağdatoğlu H, *et al.* Isolated trigeminal neuralgia secondary to distal anterior inferior cerebellar artery aneurysm. *Neurosurg Rev*, 19(1) : 43-46, 1996.

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