Case Report

Decision-making in classic trigeminal neuralgia concurrent with a pontine cavernous malformation: Causal or coincidental association?

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\section*{ABSTRACT}

Trigeminal neuralgia is classically associated with neurovascular compression of the trigeminal nerve, at the root entry zone (REZ). However, patients are occasionally affected by intra-axial involvement of trigeminal sensory fibers caused by demyelinating diseases, strokes and, rarely, pontine cavernous malformations. We discuss the management strategies and decision-making process in a 55-year-old patient, affected by trigeminal neuralgia with 2 potential causative mechanisms: a neurovascular conflict at the trigeminal REZ and an ipsilateral cavernous malformation at the pontine nucleus of the trigeminal nerve.

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La toma de decisiones en la clásica neuralgia del trigémino concurrente con una malformación cavernosa pontina: ¿causa o asociación fortuita?

\section*{RESUMEN}

La neuralgia del trigémino está clásicamente asociada con la compresión neurovascular del nervio trigémino, en la zona de entrada de la raíz (REZ). Sin embargo, los pacientes son ocasionalmente afectados por la implicación intra-axial de las fibras sensitivas del trigémino causadas por enfermedades desmielinizantes, accidentes cerebrovasculares, y raramente por malformaciones cavernosas pontinas. Se discuten las estrategias y la toma de decisiones en el caso descrito.

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decisiones en un paciente de 55 años de edad, afectado por la neuralgia del trigémino, con dos posibles mecanismos causales: un conflicto neurovascular en la zona de entrada de la raíz del trigémino y una malformación cavernosa en el núcule pontino del trigémino ipsilateral.

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**Introduction**

The classic model of trigeminal neuralgia (TN) is characterized by typical pain, normal neurological examination and association with a causative phenomenon, namely extra-axial vascular compression of the trigeminal nerve producing a slight, rather chronic damage to the trigeminal root entry zone (REZ) nearby the pons.\(^1,2\) In addition, patients are occasionally affected by the intra-axial involvement of trigeminal sensory fibers caused by demyelinating diseases, strokes, and rare pontine cavernous malformations.\(^3-11\)

Concurrent extra- and intra-axial causative mechanisms of pain generation comprise a special situation that was only described in the spectrum of multiple sclerosis\(^2\) or brainstem ischemia.\(^1\) In this regard, surgeons are particularly faced with a diagnostic dilemma as the contribution of central and peripheral mechanisms to the pathogenesis of TN remains unclear. This condition can be very challenging for decision-making concerning the best surgical treatment. In patients with multiple sclerosis or brainstem ischemia, microvascular decompression is generally associated with poor long term results, for this reason percutaneous procedures are preferred.\(^3,4\) We discuss the management strategies of a unique case, in which TN was caused by a neurovascular conflict at the trigeminal REZ associated with an ipsilateral cavernous malformation (CM) at the trigeminal pontine nucleus.

**Case report**

**History**

A 55-year-old man sought treatment for a six-year lancinating left facial pain in the territory of the second and third trigeminal nerve branches. His past history revealed systemic hypertension, with regular use of medication. The pain was paroxysmal, lasted for seconds and was evoked by touching, washing, shaving, talking, as well as brushing the teeth, with a trigger zone at the left inferior lip. Carbamazepine (200 mg twice daily) had been effective for the first years but later on he experienced no pain control despite drug augmentation to 1200 mg/day, in addition to Fenitoin (300 mg/day) and Clonazepan (3 mg/day).

**Clinical examination and diagnostic work-up**

Neurological examination revealed no abnormalities. Brain magnetic resonance imaging (MRI) (Fig. 1) demonstrated a deep-seated, poorly defined left pontine lesion, which was hyperintense on T2-weighted, and remarkably hypointense on susceptibility-weighted imaging (SWI) located on the topography of the trigeminal nucleus measuring 8.2 mm × 5.8 mm × 9 mm. The lesion was highly suggestive of a CM, however there were no signs of acute hemorrhage. MRI also revealed a volumetric reduction of the left trigeminal nerve associated to a neurovascular conflict of the left superior cerebellar artery (SCA) on 3D CISS (constructive interference in steady state) (Fig. 2). No other lesion was observed. Digital subtraction angiography showed a duplicated left SCA, without dilated arteries, or veins in the posterior fossa.

**Electrophysiological examination**

Sensory and pain perception thresholds were obtained by using bipolar electrical stimulation with surface electrodes placed on the forehead above the eyebrow (V1); on the cheek (V2) and on the chin (V3) just lateral to the mental foramen.

**Fig. 1 – Axial susceptibility-weighted imaging (SWI) gradient-echo MR images showing the cavernous malformation (arrow), with its typical low signal due to hemosiderin, located in the left lateral part of the pons.**
Constant-current square-wave electrical stimuli were delivered at a 3 Hz stimulation rate with 200 ms pulse duration and varying intensity (Medelec stimulator – Vickers Medical, UK). The patient was asked to state when stimuli of increasing current intensity became noticeable (detection threshold) and “definitely” painful (pain threshold). Thresholds were measured in all trigeminal divisions and compared to the opposite side being determined by the method of limits, in which the average was taken from six or more observations. There was no difference between the sides. Following sensory thresholds determination, blink reflex was tested according to a previously described and validated protocol. In short, single electrical stimulation was applied at intensity of 32 mA on the supraorbital nerve and responses were recorded from the inferior orbicularis oculi muscles by using surface electrodes. Waveforms were obtained from both sides and compared to each other. The first responses (R1) had latency of 10.8 ms on the right side, and 11.6 ms on the left, while the second responses (R2) were detected at 35.2 and 32.6 ms, respectively. To be considered pathological, a delay of more than 4 ms should be encountered when comparing both sides.12

**Management and postoperative course**

Since there were no electrophysiological signs of brainstem dysfunction, or active bleeding on MRI, TN was attributed to the neurovascular conflict and therefore the patient was taken to surgery for microvascular decompression (MVD). During surgery, we observed both SCAs running inferiorly to the trigeminal nerve, in which the higher one came into close contact with the trigeminal REZ before entering the cerebellum prematurely. Following careful arachnoid dissection, the higher SCA branch was freed from the nerve, and a piece of shredded Teflon felt was placed between the artery and nerve. The postoperative course was uneventful, and the patient was completely relieved from pain in the immediate postoperative period. The patient was followed for three years being without medication after a progressive reduction schema. With TN resolution by MVD, CM was considered asymptomatic. The patient was then scheduled for a clinical follow-up and imaging.

**Discussion**

Typical TN is characterized by brief shock-like pain, which is abrupt in onset and termination, being evoked by trivial stimuli and also occurring spontaneously. There is no clinically evident neurological deficit.2 Although TN is a well-defined clinical syndrome, the underlying mechanisms are still a matter of debate. At present, there is considerable evidence demonstrating that TN is caused by demyelination of trigeminal sensory fibers within either the nerve root or, less commonly, the brainstem. Demyelination mostly involves the proximal part of the root as a result of chronic compression by an overlying artery or vein. Such segmental demyelination leads to the generation of abnormal impulse transmission (ephaptic transmission), in which non-noxious stimuli abnormally activate neighboring pain fibers.1

Cavernous malformations, on the other hand, comprise angiographically occult vascular lesions occurring in any part of the central nervous system (CNS). The advent of MRI has substantially increased the number of patients diagnosed as having CM. It comprises a CNS vascular malformation affecting 0.4–0.9% of the population, which mostly occurs as an incidental finding in up to 19% of cases. Symptomatic lesions usually demonstrate evidence of recent hemorrhage in association with seizures in supratentorially located lesions, and focal neurological deficits, when located in the posterior fossa.13,14

Even though the pons is the most common CM infratentorial location, TN occurring as the first or exclusive symptom was previously reported in only seven publications to date.5–11 It is worth mentioning that from these patients, only three developed TN related to a pontine CM,6,8,11 whereas the remaining patients had CM placed elsewhere, namely intramedullary,5,10 in the interpeduncular cistern7 and at the trigeminal nerve.8

Two pontine CM-related TN5,8 had spontaneous paroxysmal pain but demonstrating atypical patterns, in which pain was not evoked by cutaneous stimuli, and, in one of them, there was some degree of facial hyposthesia and anisocoria (Table 1).

The third patient11 also experienced paroxysmal pain, unresponsive to carbamazepine, however the description about evoked pain was not provided by the original authors. Likewise, brainstem ischemic lesions involving trigeminal tracts or nuclei had been considered in the generation of severe shooting pain, in which the symptom is not usually provoked by stimulation of trigger areas. Thus, it has been suggested that patients with lesions located at REZ would develop
| Author (yr)          | Pain mechanism | CM location                  | Pain characteristics | Distribution | Neurological deficit                                                                 | Electrophysiological evaluation                  | Neurovascular conflict (MRI) | Management       |
|---------------------|----------------|------------------------------|---------------------|--------------|---------------------------------------------------------------------------------------|----------------------------------------------|-----------------------------|----------------|----------------|
| Saito et al. (1989) | Central (CM)   | Intramedullary               | P, E                | V2           | Hyperpathia, motor, and sensory deficit of limbs and body (after bleeding)             | –                                           | –                           | Surgical (CM)   |
| Shimpo (2000)       | Central (CM)   | Pontine                      | P, NE               | V1           | Anisocoria, hypoesthesia (pain and cold)                                              | Blink reflex, delayed R1 latency             | None                        | Conservative    |
| Muzumdar et al.     | Peripheral (CM)| Interpeduncular cistern     | P, –                | V2–V3        | Ptosis, diplopia, hypoesthesia                                                         | –                                           | –                           | Surgical (CM)   |
| Vitek and Tettenborn (2002) | Central (CM) | Pontine                      | P, NE               | V2           | None                                                                                   | Blink reflex normal                           | None                        | Conservative    |
| Deshmukh et al.     | Central (CM)   | Trigeminal nerve             | P, –                | V3           | Hearing loss, hypoesthesia                                                              | –                                           | None                        | Surgical (CM)   |
| Stellmann et al.    | Central (CM)   | Intramedullary               | C, –                | V1           | Ptosis, hypoesthesia                                                                   | Trigeminal SEP and Blink reflex (R1 and R2) delayed latency | –                           | Conservative    |
| Cenzato et al. (2010)| Central (CM) | Pontine                      | P, –                | V1–V2        | None                                                                                   | SPT/Blink reflex normal                       | None                        | Surgical (CM)   |

– not attributable. Abbreviations: CM, cavernous malformation; NVC, neurovascular conflict; P, paroxysmal; C, continuous; E, evoked; NE, not evoked; SPT, sensory and pain threshold; SCA, superior cerebellar artery; MVD, microvascular decompression.
typical TN, while those having lesions located at the brainstem would experience atypical TN.\textsuperscript{15}

Regarding management, since none of them were associated to a concurrent neurovascular conflict, two pontine CM-related TN were conservatively handled\textsuperscript{6,8} and when operated, treatment was therefore directed to CM mass effect.\textsuperscript{5,7,9,11} In the presented case, ipsilateral CM in a close anatomical relationship to the trigeminal nucleus could explain the occurrence of TN. However, as aforementioned, it would be expected for the patient to experience some degree of atypical pain, or at least a sensitive deficit. Instead, the pain was typical, classically without, neurovascular deficits at clinical examination, or electrophysiological brainstem impairment (sensory and pain thresholds, and blink reflex), as occurs in idiopathic TN.

Moreover, careful observation of 3D CISS images clearly revealed the neurovascular conflict in the first third of the trigeminal nerve, indicating that the peripheral mechanism could play a major role in pain genesis in our case. This assumption was further confirmed by the excellent postoperative evaluation being free of pain and medication at three years of follow-up.

Conclusions

The role of vascular compression as a causative mechanism of TN in situations, by which other factors may contribute to pain generation, can initially be challenging, but typical pain, normal clinical examination, and absence of electrophysiological brainstem impairment should lead to the peripheral mechanism of pain genesis. Therefore, MVD can be effective in patients affected by a neurovascular conflict in association with a potential secondary mechanism involving the trigeminal nucleus, like a CM.

References