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Clinical presentation of trigeminal neuralgia and the rationale of microvascular decompression

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Abstract Among the facial pain syndromes, trigeminal neuralgia has a special position for many reasons. Already described in the Romans age, the specific features of its severe symptoms, the therapeutic debate and the recent curative possibilities, make this complex pain syndrome a unique entity. The clinical onset is predominantly unilateral and is described as an electric, lancinating, focal and sharp pain. It can last seconds to minutes initially, and sometimes can last as long as 1 hour. Usually the patient is symptom-free between attacks. Later in the course of the disease, patients report dull, aching, constant pain in the same distribution as the paroxysms. The pain can be triggered by non-noxious stimuli like chewing, talking, swallowing, wind on the face, cold and light touch. Thought to be attributable to fifth cranial nerve dysfunction, the first surgical attempts aimed to interrupt nerve continuity by means of a rizohtomy, with disappearance of both pain and sensory disturbances. Further investigations claimed nerve compression by vascular structures as responsible of nervous dysfunction. Hence the attempt to perform a decompression in order to relieve the symptoms and maintain physiologic nerve function. From the successful attempts of first microvascular decompression descends the now standardised and widespread technique that is commonly used today to treat trigeminal neuralgia.

Keywords Trigeminal neuralgia · Microvascular decompression · Clinical presentation · Pathogenesis · Rationale

Introduction

Trigeminal neuralgia (TN), “tic douloureux”, or Fothergill disease, is a well-known condition that neurologists and neurosurgeons are familiar with. First descriptions of this clinical entity date back to the second century AD [1], but also Arabs had some knowledge of trigeminal neuralgia during the 11th century. The first report of medical treatment is attributed to John Locke, a British physician and philosopher, who prescribed “laxatives” to an affected patient in Paris, in 1677 [2]. One century later, Nicolas André and John Fothergill collected different series of patients. The first, who named the disease “tic douloureux”, grouped the disease with convulsions, tetanus and spasm, conceptualising them as a unique nosologic entity, claiming “vicious nervous liquids” as being the cause, and proposing the use of caustic agents for the infraorbital nerve. The latter performed a very meticulous description of the symptoms, postulating the syndrome was caused by some sort of cancer [2]. When, finally, Sir Bell in 1820 described the fifth cranial nerve, the name trigeminal neuralgia was definitely applied [3]. Due to the lack of a pathological explanation for the pain, many therapies were initially tried, such as wine assumption, rest in a dark room, laxatives or even the assumption of hemlock, opium, arsenic [2]. None of these therapies did succeed. Among drugs, some anaesthetic agents were also employed, such as trichloroethylene or stilbamidine. In a more recent past, treatment has become surgical, ranging from dental extraction (often result of misdiagnosis) [4], to chemoneurolisis (by means of direct injection of chloroform [1] and alcohol [5] in the Gasserian ganglion, or glycerol in the trigeminal cistern [6]), from radiofrequency techniques (refined only few years ago) [7–9], to trigeminal nerve compression [10, 11]. All treatments carried significant side effects (loss of sensitivity, muscle

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weakness, herpes virus infection, etc.) and early recurrence [2]. Microvascular decompression (MVD) is the treatment of choice. Radiation Therapy [1] and Stereotactic Radiosurgery [12] are a recent adjunct to the therapeutic options for trigeminal neuralgia. The latter, by means of Gamma Knife [13], assumes a peculiar interest in the light of the spreading availability of robotic frameless stereotaxy [14, 15]. Long-term results still have to be carefully evaluated with the time of long follow-up.

Physiopathology

Axons within the central nervous system are covered by myelin, which is generated by oligodendrocytes and is termed central myelin; in contrast, in the peripheral nerves, the myelin of axons is generated by Schwann cells. When a cranial nerve exits or enters the brainstem, the region of central myelin extends for a variable distance away from the brainstem and then changes into the peripheral myelin. This zone of transition is called the Obersteiner-Redlich zone. The area of the nerve that has central myelin is very vulnerable to trauma caused by the repeated pulsation of an artery in contact with the nerve. This process of nerve root injury may then cause demyelination [16, 17] over a focal area and an abnormal conduction or short-circuiting within the axons, which is called ephaptic transmission. This abnormality may lead to the production of a variety of hyperactive cranial nerves syndromes. Ectopic action potential generation in the sensory root of the nerve may be responsible for the typical, episodic, electric, lancinating pain of the trigeminal neuralgia [18, 19]. Relief of vascular compression leads to a permanent cure in a high percentage of patients, without permanent deficits in the distribution of the cranial nerve [20]. As shown by intraoperative electrode recordings, improvement in trigeminal nerve conduction after decompression, corroborates evidence that compression of the trigeminal nerve by a blood vessel is the major causative factor [21–23].

Clinical presentation

The diagnostic criteria for trigeminal neuralgia have to be all searched in the patient's clinical history. Pain is perceived in one or more divisions of the trigeminal nerve, mostly unilaterally. Pain is shooting, lancinating, sharp, agonising and described as an electric shock. Usually lasts seconds to minutes with repetitive bursts every few seconds. The patient is symptom-free between the attacks. A common evidence can be the trigger effect of some routine actions involving territories innervated by the affected root, such as speaking, swallowing, chewing, brushing the teeth, or sensitive stimuli applied in these regions like sim-

ple light touch, cold, or an air blow. Even a simple position of the head can trigger the pain. Lying down over the painful area can worsen an attack; in the same manner, reversing the position can improve it. The trigger stimulus, applied to the "trigger zone", often arouses intense pain in divisions beyond the one stimulated. This allodynia is A-beta fibre activity with neuronal reorganisation at the level of dorsal root ganglion and rostrally [24]. The sensation is so discouraging that indeed even simple behaviours or activities are inhibited and social relations are compromised. A sense of despair can lead the patient to commit suicide. If untreated, or unsuccessfully treated, later in the course of the disease patients experience dull, aching, throbbing or burning, constant pain in the same distribution as the paroxysms. A long interval between the attacks is often described as a period of increasing paresthesias in the nerve distribution. In a minority of cases, pain can be experienced in the external auditory canal. Patients can describe a clicking sensation in the omolateral ear, possibly due to the motor innervation of the tensor tympani muscle.

Family history is present in about 5% of patients with trigeminal neuralgia. Up to 5% of patients can complain of bilateral, sequential pain. In our series, according to the literature, there was a female prevalence, in the sixth decade. The age range at presentation was 21 to 90 years. There is some controversy about the frequency of side of presentation and number of divisions involved [25]. In our series the right side was most frequently involved (56%) and maxillary branch was most frequently affected. Only in 13% all divisions were involved.

McGill Pain Questionnaire (MPQ) is commonly used to rank trigeminal neuralgia in affected patients. Beyond strictly evaluation of painful sensation, it can give a reliable indication of the affective stress.

Diagnostic clues

An accurate examination of the fifth cranial nerve starts exploring corneal sensitivity with a fine tip of a cotton swab, touching the cornea to elicitate the corneal reflex, considering that the upper half of the cornea is innervated by V₁, the lower by V₂. The sensory examination has to be performed on all three divisions: exploration of light touch (cotton wool), pinprick, hot/cold sensation, and deep pressure allow to discriminate a sensory deficit often present, but not described by the patient [26]. Distal small-fibre loss with neuropathy produces the feeling of burning pain. The sensory loss may not always be in the same area of the pain. Jannetta described a high incidence of hyperesthesia to cotton wool in the area of the nasolabial fold ipsilateral to the pain. Nurmikko and Eldridge in 2001 showed that electrophysiological investigations documented sensory trigeminal nerve abnormalities in the triggered zone [24]. Lunsford et al., by means

of evoked potentials, related nerve fibre dysfunction to the pain, finding that 86% of patients had nerve conduction abnormalities. Furthermore, 83% improved after microvascular decompression.

Tactile and temperature thresholds are raised in trigger areas, and hyperalgesia is often a response to normothermal stimuli [27]. There is often temporal summation (abnormal increases in intensity of pain to constant-strength stimulus, radiation of pain from the stimulus, after-sensation). Temporal summation of pain is a hallmark of central hyper-excitability to pain. Allodynia and hyperalgesia are the hallmarks of neuropathic pain. These findings implicate peripheral fibres involvement in trigeminal neuralgia [24]. Electrophysiological investigations of the trigeminal nerve have yielded consistent results, but they have not been widely used [16].

Imaging

It is well-established that typical trigeminal neuralgia is caused by a neurovascular conflict. A cornerstone in the history of trigeminal neuralgia was the possibility to visualise a tight relationship between the apparent origin of the fifth cranial nerve and some vascular structures. While the conventional T₁ and T₂ Magnetic Resonance Imaging (MRI) are useful in the differential diagnosis, excluding space-occupying lesions of the fifth nerve or close to it, specific angiographic MR algorithms allow 90.5% sensitivity with 100% specificity of vessel compression [28]. Nevertheless, the correlation of imaging with intra-operative findings has been reported to be 82.6%, 67%, 80%, 71% in various series, according to different MR sequences [29, 30]. In our series, 104 patients suspected having a neurovascular conflict for trigeminal neuralgia underwent MRI-3D CISS (constructive interference in steady state), obtaining images of the posterior fossa reconstructed using multiplanar reconstruction (MPR) algorithms. TOF (time of flight)-3D MRI angiograms of the posterior fossa were also taken and reconstructed with maximum intensity projection (MIP) algorithms. With these sequences, the vascular contact was accurately identified: the superior cerebellar artery (SCA) was compressing the trigeminal nerve in 80% of cases, the anterior-inferior cerebellar artery (AICA) was responsible in 15% of cases, in 4% of cases both SCA and AICA were involved and in 1% the vertebral artery (VA) only. MRI was negative in 1 case. In all our cases, but one, the neurovascular conflict was identified intraoperatively.

Differential Diagnosis

Typical trigeminal neuralgia is easily diagnosed. Neurological examination is usually normal in affected patients. However, there are reports in the literature of

many patients with TN who experienced pain for several years before receiving an accurate diagnosis [24]. While well-acquainted by neuroscientists, trigeminal neuralgia is often referred to general practitioners or dentists who are not very familiar with such a disease, leading to misdiagnosis. Pain along one or more division/s of the fifth cranial nerve, may be an atypical trigeminal neuralgia or atypical facial pain. Indeed the term “atypical” contains the concept of multiple different clinical entities. Eller et al. [31] proposed to use the “atypical facial pain” term to indicate facial pain in the context of a somatoform pain disorder, usually bilateral, spreading outside the trigeminal distribution, often associated to multiple pain complaints in other body regions, including diagnostic clustering such as fibromyalgia or chronic fatigue syndrome. Psychological testing prior to confirmation of this diagnosis should be performed. Moreover, they proposed a classification of trigeminal neuralgia (TN) according to seven diagnostic criteria from patients’ complaints [31]. TN1 and TN2 differ only for the lasting of the pain, being episodic and brief in the first, and continuous and dull in the latter that sometimes hides a tumour, cyst, vascular malformation, etc. and demands for further imaging studies. Small infarcts and other vascular lesions in the pons or nerve root can cause pain. A different group includes pain from nervous lesioning, like in trauma or surgery, neurectomy, gangliolysis, rhizotomy, nucleotomy, tractotomy, or other denervating procedures (de-afferentation pain). Trigeminal neuralgia may be associated with Multiple Sclerosis (MS) in patients, often under 40 (1%). The supposed mechanism is similar to the real trigeminal neuralgia’s one, but the pain can be constant from the beginning. In the post-herpetic trigeminal neuralgia the first division is commonly affected and is marked by the development of allodynia superimposed on a burning, constant and deep dysesthesia. Trophic changes may be noted.

In the differential diagnosis neoplastic, inflammatory, and vascular causes can be easily ruled out. Some conditions must be accurately considered: the glossopharyngeal neuralgia which is characterised by severe, stabbing pain in the ear, throat or both while swallowing; the geniculate neuralgia with a typical severe, “ice-pick” pain deep in the ear in a constant background pain. Migraine is usually unilateral, throbbing, pulsating, usually involving cranial vault, also associated with nausea, vomiting, and photophobia, seldom with aura. Sharp-like pain has an odontogenous origin and is short-lasting. Sinusitis of the maxilla causes an aching, throbbing pain in the cheek, which gets worse in the morning and improves in head-up position. Giant cell arteritis is often accompanied by malaise, diffuse tenderness, rubor in the temporal region extending to the neck. Temporomandibular joint disorders cause a dull regional ache, non radicular in distribution, often worsen by pressure and movement, and limitation of jaw opening.

Surgery: Microvascular Decompression technique (MVD)

This technique has been introduced by Peter Jannetta in 1967 [32, 33]. After anaesthesia is induced and intubation is performed, the patient is placed in the lateral position with the neck minimally stretched, flexed and rotated contralateral to the pain side. The mastoid eminence, digastrics groove, and inion should be identified and an inio-meatal line drawn to define the transverse sinus. A vertical or “italic S”-shaped incision is drawn 3- to 5-cm long, approximately 0.5-cm posterior (medial) and parallel to the hair line. After soft tissues opening and bone preparation, burr hole is performed approximately on the mastoid emissary vein; the asterion can be a useful landmark. The goal of bone exposure should be to identify the edge of the junction of the transverse and sigmoid sinuses first, in order to obtain a small and safe craniectomy. The junction of the transverse and sigmoid sinuses must, then, be visualised. A T-shaped incision is made in the dura mater to expose the most superior and lateral corner of the dura adjacent to the junction of the transverse and sigmoid sinuses, to allow a direct corridor along the petro-tentorial bone. At this point the cerebellopontine angle has to be exposed. The surgeon should allow some drainage of cerebrospinal fluid (CSF) in order to minimise the cerebellar retraction. On entering the cerebellopontine angle, the first structure visualised will be the seventh-eighth nerve complex, located superficially and caudal to the trigeminal nerve. The trigeminal nerve is located in the most superior and deepest position. Decompression is relatively straightforward if the surgeon keeps in mind that the dorsal root entry or exit zone can be variable in length, particularly in the case of the nerve, and may extend to a more distal portion of the nerve itself. Therefore, the nerve should be inspected from its origin at the brainstem laterally to its exit from the cerebellopontine angle, and all vessels should be visualised. The compression may be proximal or distal, and it may be located under the ala of the cerebellum. Microvascular decompression of the trigeminal nerve requires sharp dissection of all arachnoid around the trigeminal nerve and superior cerebellar artery which usually compresses the nerve either at the brainstem or distally. Rostral compression of the nerve causes pain in the V_3 , and this is most commonly due to the SCA looping downward and upward again. As the artery elongates, it compresses the middle portion of the nerve, causing pain in the V_2 in addition to the V_3 . The relatively rare, isolated pain in the V_1 is caused by a vessel on the caudal side of the nerve. Isolated pain in the V_1 is most common in older men, cigarette smokers, and patients with dolichocephalic features, in whom the vertebrobasilar system arteries compress the nerve from the caudal side. Isolated pain in the V_2 is most common in younger women and is caused by a bridging vein that may be quite distal on the nerve. After the arachnoid is dissected, the looping ves-

sel can be mobilised in order to interpose a piece of muscle or shredded Teflon felt in between. Even without evident microvascular conflict, a simple explorative procedure with mobilization of neurovascular structures of the area, may result in symptoms remission. Tight dural closure is important to ensure watertight closure. The bone edges of the mastoid air cells are accurately waxed. The deep and superficial muscles are approximated. The fascial closure must be watertight to prevent any CSF leakage. Most frequent complications are cerebellar injury, hearing loss, and CSF leakage. Rare complications of the procedure, are facial weakness or anaesthesia and lower cranial nerve dysfunction. The entire decompression procedure (from skin incision to skin closure) generally takes less than 2 hours and requires only a small corridor of exposure between the cerebellum and petrous temporal bone. This corridor is kept to a minimum by adequate exposure of the sigmoid sinus through mastoid bone removal prior to durotomy. This allows a dural incision very close to the sigmoid sinus rather than a more posterior durotomy that requires more cerebellar retraction to permit visualization along the petrous temporal bone. Avoidance of CSF leaks remains problematic after transgression of mastoid air cells and exposure of multiple overlapping tissue planes. Our incidence of CSF leaks has declined since 1990 from 3.65% to 2.15% ($p < 0.01$). Great attention must be paid to mastoid air cells: it is compulsory to fill them with abundant bone wax. The nuchal musculature has to be tightly sutured before fascia is closed. Postoperative CSF leaks usually resolve with lumbar drainage, only a minority of cases requires operative intervention, including re-exploration of the dural closure and careful inspection of the mastoid air cells. Surface veins cause a special problem, because they are prone to recollateralise if coagulated and divided. Most early recurrences are the result of these recollateralised veins. Subsequent recurrence (0.5%/year) is due to new blood vessels, especially arteries, pressing on the nerve, as a result of the continuation of the aging process.

Conclusion

The natural history of TN indicates progressive large-fibre loss, making some therapeutic options poorly effective. Many treatment strategies are available today: among them, microvascular decompression is the gold standard treatment. The commitment of neurosurgeons in this area has led to a progressive refinement of the technique over the years, with significant reduction of post-operative mortality and morbidity and indication also for elderly patients [34]. Furthermore, concerning the mechanism of the radicular damage, intra-operative electrophysiological studies allow us to exactly assess the damaged fibres, responsible of specific symptoms and signs. These elegant complementary studies allow to character-

ize patients with trigeminal neuralgia according to the damage of large-fibre, small-fibre, or mixed sensory neuropathy. This may lead to more precise surgical procedures in which the appropriate fibre group is targeted [2].

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