Physica Medica 30 (2014) 592–595

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Radiosurgery in trigeminal neuralgia

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ARTICLE INFO

Article history:
Received 15 January 2014
Received in revised form
13 May 2014
Accepted 14 May 2014
Available online 2 June 2014

Keywords:
Trigeminal neuralgia
Treatment options
Radiosurgery
Mechanisms

ABSTRACT

Trigeminal neuralgia is a rare but debilitating pain syndrome with a distinct clinical presentation mainly affecting people advancing in years. Compression of the trigeminal nerve by an aberrant vascular loop has been proposed as the causative factor in the majority of cases leading to the development of a highly effective surgical treatment approach termed "microvascular decompression". Nevertheless the mainstay of treatment remains medical. This article gives a brief overview of current treatment options for trigeminal neuralgia with special emphasis on radiosurgery. Possible mechanisms underlying the therapeutic effect of radiosurgery are discussed with some consideration of implications for optimizing prescription dose and target definition.

Historical background

As its name implies trigeminal neuralgia refers to a neuropathic condition involving cranial nerve V. It is characterized by the frequent occurrence of paroxysms of severe pain felt unilaterally in the distribution of the trigeminal nerve alternating with periods of complete absence of pain and usually follows a chronic course with spontaneous remissions being the exception rather than the rule. The onset of the condition is usually in adult life with children being rarely affected. Because of the excruciating and ongoing nature of pain attacks trigeminal neuralgia ranks among the most painful conditions known to mankind to the point where the deliberate ending of one's life may be seen as the only effective means of escape from suffering. Because of its association with this very sad outcome trigeminal neuralgia has also come to be referred to as the "Suicide Disease". Accounts of this pain syndrome can be traced back to the earliest part of the recorded history of medicine giving testament to the great burden of suffering imposed by it upon mankind. The first succinct description of the condition was given by John Fothergill, an English physician who lived in the 18th century and who apart from recognizing the paroxysmal nature of the pain as well as a female preponderance also stressed the fact that the pain could usually be elicited by "triggers" such as eating, talking or shaving. It wasn't, however, until the groundbreaking work of Sir Charles Bell, a 19th century Scottish surgeon, anatomist and neurologist who unraveled the separate functions of the trigeminal and facial nerves, that a dysfunction of the trigeminal nerve could be established as the anatomical substrate underlying trigeminal neuralgia [1].

Epidemiology and clinical picture

Trigeminal neuralgia is a rare condition with an incidence of about 2–5/100,000/year. There is a progressive increase of the incidence with age reaching values of up to 25.6/100,000/year for people aged 70 or over. Women are known to be more commonly affected than men [2].

The main clinical feature of classical trigeminal neuralgia is the occurrence of discrete bouts of sharp, lancinating, "electric shock"-like facial pain that is limited to one side of the face, i.e. the distribution of the sensory fibers of the trigeminal nerve. Attacks are frequently preceded by an identifiable stimulus such as brushing teeth, shaving or even noise but there is usually no pain whatsoever between attacks, a feature that is very helpful in distinguishing it from other pain syndromes affecting the head area. The second and third divisions that supply sensation to the cheek and jaw are the most commonly affected while the forehead which derives its innervation from the first division is frequently spared. Pain is not only felt in the skin of the affected areas but also inside the mouth and the sinuses thereby mimicking dental problems frequently leading to diagnostic confusion and sometimes even culminating in unnecessary root canal procedures or tooth extractions.

It is now recognized that apart from the classical picture just described, there is also another much rarer presentation of trigeminal pain that differs from the classical variant in many

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http://dx.doi.org/10.1016/j.ejmp.2014.05.006
1120-1797/

important ways. In this atypical form of the condition the pain is not sharp but rather aching, crushing or burning in quality. Although its intensity tends to fluctuate it never goes away completely. Distinct attacks of pain that are so characteristic of the classical type do not occur. Because of this, diagnosis tends to be more difficult and response to treatment is also poorer than in classical trigeminal neuralgia [3].

Etiology

Although trigeminal neuralgia may be secondary to underlying pathology such as shingles (post-herpetic neuralgia), demyelinating disorders such as multiple sclerosis or space occupying lesions such as cerebellopontine tumors or arachnoid cysts, in the majority of cases this is not true.

Classical trigeminal neuralgia is thought of today as a "vascular compression syndrome". This insight is owed to observations made by Walter Dandy, an American neurosurgeon who operated on a large number of patients with trigeminal neuralgia using nerve transection which was popular among neurosurgeons during the first half of the 20th century. He noticed that in the majority of patients there was an aberrant vascular loop that was given off by the superior cerebellar artery and that was abutting the nerve near the point where it exits the brainstem. It is presumed that due to its incessant pulsations this aberrant arterial loop is able to cause chronic injury to the myelin sheath and that this then leads to ephaptic signal transmission and spontaneous neural activity thus explaining how clinical symptoms arise [4].

Despite these advances in our understanding of the underlying pathophysiology of the condition diagnosis remains essentially clinical. History-taking tries to elicit the characteristic clinical features previously described while the importance of a thorough physical examination and the acquisition of a brain MRI consists not so much in confirming the clinical diagnosis as in ruling out underlying pathology such as mass lesions, multiple sclerosis or aneurysms.

Treatment options

Treatment options for trigeminal neuralgia are many and varied. Because of its promise of rapid and uncomplicated symptomatic relief medical treatment is usually seen as the first choice. Anticonvulsant medications such as carbamazepine, phenytoin or lamotrigine have proven clinical benefit with carbamazepine being effective in about 90% of cases. By blocking membrane sodium channels they are known to enhance electrical stability of cell membranes and to suppress erratic signaling offering a good explanation for their effectiveness in the treatment of neuropathic pain states such as trigeminal neuralgia. If symptoms cannot be sufficiently controlled with one of these drugs, drugs with different mechanisms of action may be tried. These include amitriptyline, pregabaline, baclofen and oxycodone. The main disadvantage of the medical approach is that the treatment is purely symptomatic and that there is no effect beyond the time during which the drug is present in the body at therapeutic concentrations. Lifelong treatment is therefore usually necessary. Unfortunately there is frequently a decline in the drug's effectiveness over time requiring repeated increases in dose while at the same time dose-limiting side effects may occur. These may be severe including bone marrow and liver toxicity as well as neurological side effects such as drowsiness, double vision and ataxia [5].

For this reason sooner or later more definitive treatment options will be needed in a large proportion of patients. These treatments are all essentially surgical and all target the anatomical area thought to be involved in symptom generation, i.e. the intracranial part of the trigeminal nerve. Surgery can be performed "open", "minimally invasive" using percutaneous procedures or even "non-invasive" using radiosurgery.

Open surgery

Open surgery nowadays employs a technique that has come to be known as "microvascular decompression". In this procedure, pioneered by the American neurosurgeon Peter Jannetta and based on the assumption that compression of the nerve by a vascular loop is the direct cause of the problem the neurosurgeon by making a small opening in the skull first obtains access to the trigeminal nerve where it exits the brainstem. The aberrant vascular loop is then identified and separated from the adjacent trigeminal nerve. Following this, a small Teflon pad is placed between the nerve and the vascular loop to prevent chafing of the loop against the nerve in the future [4]. The success of this procedure has been evaluated in a large number of patients lending credence to the vascular compression theory. In the largest patient series with a total of 1185 patients and a median follow-up of 6.2 years published by Jannetta himself, the reported initial success rate was as high as 98% with 82% of patient becoming completely pain-free. At ten years 70% of patients remained free from symptoms. Considering that microvascular decompression requires open surgery the complication rate in this series was relatively low with death occurring in 0.2%, brainstem infarction in 0.1%, hearing loss in 3% and facial weakness in 0.5% [6].

Percutaneous minimally invasive procedures

In patients who are not candidates for open surgery minimally invasive percutaneous procedures may be tried. Unlikely microvascular decompression they are all ablative, i.e. they work through causing destruction of nerve fibers and therefore cause facial anesthesia to varying degrees.

Radiofrequency rhizotomy uses thermal energy to damage preganglionic trigeminal rootlets. It may give immediate pain relief in up to 97% of cases with a 42% recurrence rate at 5 years. As might be expected from an ablative procedure pain relief is dependent upon the depth of facial anesthesia [7,8].

In glycerol rhizotomy glycerol is injected percutaneously into the retrogasserian portion of the trigeminal nerve causing chemical damage to sensory nerve fibers. It is able to achieve good or excellent outcome in 60–83% of cases at 1 year but recurrence rate at 6 years has been reported as high as 92%. Main complications include corneal disturbance from anesthesia of the first division of the nerve (5–24%), facial hypoesthesia (3–33%) and anesthesia dolorosa (0–5%) [9].

In balloon compression an inflatable balloon is inserted percutaneously to the area around the Gasserian ganglion. Inflation of the balloon by exerting pressure on the nerve then causes mechanical damage to nerve fibers. This procedure has reported success rates of around 90% with recurrences during follow-up in about 30%. Marked facial numbness may follow and there is often transient weakness of the muscles of mastication on the affected side. There is usually better sparing of corneal sensation than in glycerol rhizotomy [8].

Radiosurgery

It may come as a surprise that the concept of using ionizing radiation to treat trigeminal neuralgia dates back nearly to the discovery of X-rays themselves when their therapeutic potential was just starting to be recognized by the medical profession. Hermann Moritz Gocht (1869–1938), a German radiologist and