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Trigeminal Neuralgia Secondary To Sclerosteosis: Clinical Picture Of Various Treatment Modalities

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Abstract

Background: Sclerosteosis was first described by Hirsch in 1929 and defined by Hansen in 1967. Trigeminal neuralgia is the most difficult neuropathic pain to treat. The purpose of this narrative review is to discuss the various treatment modalities for trigeminal neuralgia in sclerosteosis patients.

Methods: Many relevant papers within Academia.edu, PubMed, ResearchGate, ScienceDirect, and EMBASE were searched for, taking into consideration publications up to 2019. Additional research was done through relevant books.

Results: Trigeminal neuralgia secondary to sclerosteosis presents with proximal facial pain. Dedicated diagnostic tests such as MRI and CT are required to identify any tumor or blood vessel compressing the trigeminal nerve. Patients with sclerosteosis present with a narrowing of the foramen ovale on CT. Although no extensive research has been done, according to an expert opinion, no drugs have proved to be promising in treating trigeminal neuralgia in sclerosteosis patients. Surgical procedures that give positive results include percutaneous balloon compression, CT-guided percutaneous rhizotomy, and stereotactic radiosurgery.

Conclusions: The resistance to drugs makes them of no use in the treatment of TN in SC patients. MVD is considered a "gold standard" in the treatment of TN but has proved to be of no use in SC, as pain is of diversified nature. Percutaneous techniques have proved to be a good option, but the narrowing of the foramen ovale makes it a challenge for surgeons. RFR is an effective treatment option but has many side effects. CT-PR facilitates easy placement of the needle and can be employed. SRS has promising results, but to date, no research has been published concerning the procedure.

Keywords: sclerosteosis, trigeminal neuralgia, facial pain

Background

Sclerosteosis (SC) was first described by Hirsch in 1929 and defined by Hansen in 1967. It is a rare disorder that leads to the overgrowth of bones. Facial nerve palsy and neuropathic pain are common symptoms in patients with SC. The most difficult type of neurological pain to treat is trigeminal neuralgia (TN). The purpose of this narrative review is to discuss the various treatment modalities for TN in SC patients.

Methods

Many relevant papers within academia.edu, pubmed, researchgate, sciencedirect, and EMBASE were searched for, taking into consideration publications up to 2022. Additional research was done through relevant books. All searches used the subsequent keywords: sclerosteosis, trigeminal neuralgia, and facial pain. The first search was supplemented by a secondary search. The search is limited to the English language. This search yielded approximately 200 articles, which were reviewed by title and abstract for potential relevance to the subject.

Results

Definition

Sclerosteosis- is a very rare autosomal dominant disorder caused by inactivating mutations in sclerostin. Sclerostin is the product of the SOST gene, located on chromosome 17q12-q21. This results in overgrowth of bone due to enhanced osteoblastic activity with a failure of osteoclasts to compensate for increased bone formation.

Trigeminal Neuralgia- also called Fothergill disease or Tic Douloureux, is a pain disorder affecting the trigeminal nerve. It is a type of neuropathic pain commonly involving the maxillary (V2) and mandibular (V3) branches of the trigeminal (5^{th} cranial) nerve.

Classification

Sclerosteosis- is of two types:

SC1/SOST1- Related to Van buchem disease and craniodiaphyseal dysplasia. The gene associated is SOST. Affiliated tissues include bone, medulla, and bone marrow. Related phenotypes are frontal bossing; nystagmus

SC2/SOST2- Related to SC1 and Myasthenia Gravis. The gene associated is LRP4 (LDL Receptor Related Protein 4). Affiliated tissues include bone. Related phenotypes are frontal bossing, and macrocephaly

Trigeminal Neuralgia- Based on symptoms:

1. Typical TN- due to blood vessels compressing the trigeminal nerve root

2. Atypical TN- due to vascular compression of a specific part of the trigeminal nerve

International Classification of Headache Disorders (ICHD) for TN is given in figure 1.

Burchiel's classification of TN is given in figure 2.

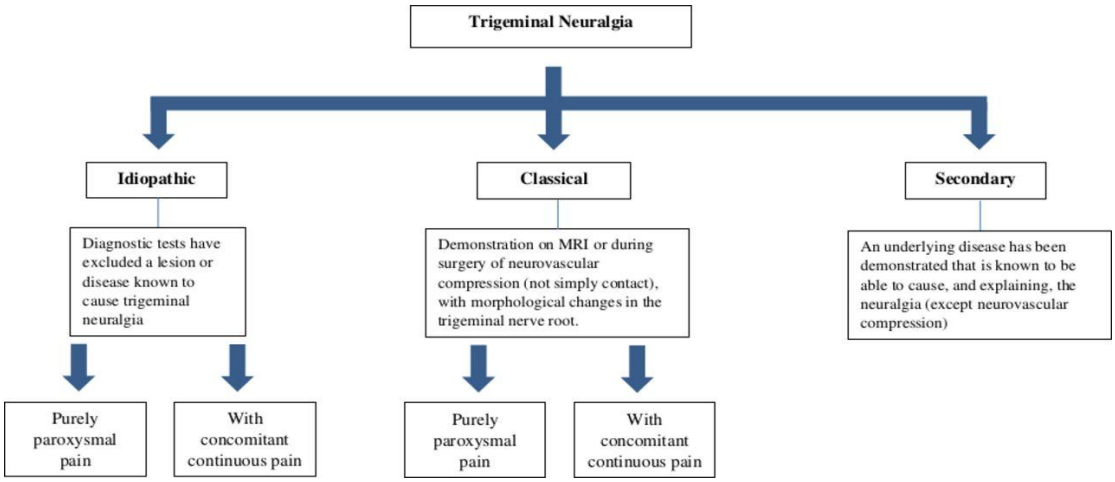

Figure 1: ICDH Classification of Trigeminal Neuralgia

Burchiel classification	History
Spontaneous onset	
TN, Type 1	>50% episodic pain, sharp, shooting, electrical shock-like
TN, Type 2	>50% constant pain, aching, throbbing, burning
Trigeminal injury	
Trigeminal neuropathic pain	Unintentional, incidental trauma
Trigeminal deafferentation pain	Intentional deafferentation
Symptomatic TN	Multiple sclerosis
Postherpetic neuralgia	Trigeminal Herpes zoster outbreak
Atypical facial pain	Somatoform pain disorder

TN, trigeminal neuralgia.

Figure 2: Burchiel's Classification of Trigeminal Neuralgia

Clinical Characteristics

Sclerosteosis- Patients present with:

1. Syndactyly of the index and middle fingers
2. Recurrent facial nerve palsies
3. Facial pain due to 5th cranial nerve (CN) palsy
4. Visual loss due to 2nd CN palsy
5. Hearing loss in children and adults due to 8th CN palsy
6. Increased intracranial pressure
7. Gigantism, prominent square mandible, broad flat nasal root, dental malocclusion
8. Midface hypoplasia, hypertelorism, frontal bossing, enlarged head circumference
9. Dysplastic or absent nails
10. Anosmia or hyposmia, proptosis

Trigeminal Neuralgia- Patients present with-

1. Severe facial pain on one side of the face that lasts for seconds to minutes to hours is followed by pain-free periods
2. Pain can be exploding, shooting, or stabbing
3. A burning sensation that may be constant
4. Pain can be triggered by brushing, speaking, shaving, eating or drinking, touching the face, a breeze on the face

Trigeminal Neuralgia in Sclerosteosis- Patients present with:

1. Proximal facial pain
2. Loss of vision
3. Hearing difficulty
4. A progressively increasing headache
5. An electric-shock-like sensation
6. Anosmia

Diagnostic Tests

Sclerosteosis- Radiographs- show a wide skull, thick cortices around long bones, a dense pelvis, ribs, or tubular bones

CT (Computed Tomography)- shows fusion of ossicles, narrow internal auditory and medullary canals, wide diaphyseal cortices, and osteosclerosis of the skull base, facial bones, pelvis, ribs, or vertebrae

Lab Findings- increased alkaline phosphatase, marked increase in bone formation and resorption markers, serum calcium, phosphorus, and parathyroid hormones are normal

Molecular Genetic Testing- to spot biallelic pathogenic variations in SOST

Dual Energy X-ray Absorptiometry- to detect high bone mineral density

PCR Amplification and Sequencing- of exons of the SOST gene

Trigeminal Neuralgia- Diagnosis relies purely on clinical symptoms. According to ICHD-3, the diagnostic criteria are:

1. Recurrent paroxysms of unilateral pain in the distribution of one or more divisions of the trigeminal nerve, with no radiation beyond, and fulfilling criteria 2 and 3
2. Pain has the following:
    - lasting from a fracture of a second or 2 minutes
    - severe intensity
    - electric shock-like shooting, stabbing, or sharp in quality

3. Precipitated by innocuous stimuli within the affected trigeminal distribution
4. Not better accounted for by another ICHD-3 diagnosis

MRI (Magnetic Resonance Imaging)- to detect any tumor, sclerosis, or secondary TN
3D MRI- to detect whether a vessel is compressing the trigeminal nerve

Treatment of Trigeminal Neuralgia in Sclerosteosis

Pharmacological Treatment

The resistance to medications makes their use in the treatment of TN in SC patients a failure. However, drugs that suppress bone resorption, such as bisphosphonates, denosumab, and selective estrogen receptor modulators, should be avoided. Drugs that stimulate bone formation, such as terparatide, romozosumab, and abaloparatide should also be avoided.

Surgical Treatment

Microvascular Decompression (MVD)- It is a "gold standard" in TN patients but is avoided in SC patients, although it has long-term pain relief. This is because of the difficulty encountered due to prominent hyperostosis near the base of the skull. MVD can be dangerous when performed in patients with decreased cranial capacity and increased intracranial pressure, which is a prominent feature in SC. Another reason for not performing MVD in TN secondary to SC is that TN is caused due to narrowing of the neurovascular foramen and not neurovascular conflict.

Percutaneous Retrogasserian Glycerol Rhizolysis (PRGR)- It is not performed due to the narrowing of the foramen ovale and difficulty in its identification.

Radiofrequency Rhizotomy (RFR)- It is considered the second most effective treatment in controlling pain due to TN. But is not employed due to the side effects, which include facial numbness, keratitis, corneal hypoesthesia, and anesthesia dolorosa.

Percutaneous Balloon Compression (PBC)- Provides good pain relief and has very few side effects when compared to PRGR and RFR. The shape of the balloon plays an important role. Pear-shaped balloons provide a high degree of pain relief. The only side effect known is immediate post-operative transient masseter weakness.

CT-guided Percutaneous Rhizotomy (CT-PR)- along with 3D imaging reconstruction- facilitates easy needle placement. It has very few complications.
Stereotactic Radiosurgery (SRS)- It is less invasive as there is no need for a foramen ovale puncture, craniotomy, or any incisions. The SRS technique uses 3D imaging to target high doses of radiation to affected areas with a minimum impact on surrounding healthy tissues. It is a very precise technique with fewer side effects. The maximum radiation dose employed is 70-90 Gy. A dose greater than 90 Gy causes facial numbness and radiation-induced neoplasia.

Conclusion and prospects for the future

The resistance to drugs makes them of no use in the treatment of TN in SC patients. MVD is considered a "gold standard" in the treatment of TN, but has proved to be of no use in SC, as pain is of a diversified nature. Percutaneous techniques have proved to be a good option, but the narrowing of the foramen ovale makes it a challenge for surgeons. RFR is an effective treatment option but has many side effects. CT-PR facilitates easy placement of the needle and can be employed. SRS has promising results, but to date, no research has been published concerning the procedure.

Abbreviations

TN- Trigeminal Neuralgia; SC- Sclerosteosis; CN- Cranial Nerve; CT- Computed Tomography; ICHD- International Classification of Headache Disorder; MRI- Magnetic Resonance Imaging; MVD- Microvascular Decompression; PRGR- Percutaneous Retrogasserian Glycerol Rhizolysis; RFR- Radiofrequency Rhizotomy; PBC- Percutaneous Balloon Compression; CT-PR- CT guided Percutaneous Rhizotomy; SRS- Stereotactic Radiosurgery

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