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ORIGINAL ARTICLE

Association between Trigeminal Neuralgia and Multiple Sclerosis: Role of Magnetic Resonance Imaging

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ABSTRACT

Background: Trigeminal neuralgia (TN) is a severe neuropathic unilateral facial pain affecting about 30% percent of the world population. Neuropathic pains are considered to be associated with multiple sclerosis (MS).Multiple sclerosis is a chronic inflammatory condition causing demyelination and degeneration of axons in central nervous system.

Objective: The objective of the study is to determine role of Magnetic Resonance Imaging to find association between trigeminal neuralgia and multiple sclerosis.

Methods: The prospective cohort study was conducted for six months in Radiology Department of Hayatabad Medical Complex, Peshawar from September 2020 to February 2021. Initially 250 patients were screened for multiple sclerosis. The study recruited a total of 35 patients of MS visited neuroradiology department, out of which 26 patients were enrolled in the study. The participants with age of 18 years and onward of both genders with definitive symptoms of TN with MS that is having unilateral TN pain (that is sharp shooting electric pulse like) lasting for up-to 2minutes precipitated with an environmental stimulus were included in the study. The patients (n=6) with bilateral MS with TN and cognitive disturbances (n=3) were excluded from the study.

Results: The study recruited a total of 26 participants with MS related TN. The clinical examination didn't show any difference between the three groups with the p-value less than 0.001. Age at the onset of MS was younger in patients with MS related sensory disturbances compared to other two groups, with p-value less than 0.05. The frequency of the affected side was different in all three groups with the p-value less than 0.05 as tested by Fischer exact test. Trigeminal reflex tests done for different components such as R1 and SP1 showed longer latency periods for the affected side after stimulation and unaffected side after stimulation with the mean of 14.2± 4.4 and 15.3±3.2, 16.3±4.2 and 17.4±5.2ms and p-value less than 0.001 as shown by Wilcoxon test.

Conclusion: The study showed significant association between trigeminal neuralgia and multiple sclerosis with the greater efficacy of using MRI as imaging technique to find this association.

Keywords: Multiple sclerosis, Magnetic Resonance Imaging, Trigeminal neuralgia

INTRODUCTION

Trigeminal neuralgia (TN) is a severe neuropathic unilateral facial pain affecting about 30% percent of the world population. Neuropathic pains are considered to be associated with multiple sclerosis (MS)(1). Multiple sclerosis is a chronic inflammatory condition causing demyelination and degeneration of axons in central nervous system. This type of demyelination sometimes occur in trigeminal nerve root and form plaques which effect the entry zone of root in the pons of the brain(2). The prevalence of TN with multiple sclerosis ranges from 1.9% to 4.9%.A total of 1% to 2% of TN occur in MS patients due to the demyelination plaques in pontine pathway and 10% of TN occurs due to the cerebellar pontine masses invading the nerve root(3).

Different studies have been conducted to check the relation between the TN and MS.A systematic review of pain in Multiple Sclerosis showed a prevalence of 3.8% of Trigeminal Neuralgia and it is lower than neuropathic pain or headaches(4, 5). Another study showed that patients with MS used 30% mediations for pain. The clinical signs and symptoms of TN with MS are same but sometimes different or atypical features occur in different people that is prolong background pain.(6) Previous studies reported that some patients had initial pain which increased with time and involved both sides of the face(7). Also the studies reported that background pain was not associated with demyelination plaques as viewed by MRI, while some reported the presences of increased demyelination plaques with increased episodes of pain(8).

It is considered that MS precedes TN but some studies showed that TN pain is the first appearing symptom between intervals of five to ten years before another symptom or MS symptoms appear.(9) No correlation between the extent of clinical manifestations and plaques has been observed in MRI. There is no data present that could show the periods of remission of MS symptoms(10). Trigeminal refluxes including blink reflex are normal in MS patients however the electro and neurophysiological testing of the reflexes is accurate in differentiating between typical TN and MS related TN(11).

A previous study suggested that in some patients the plaques resulting in the TN related to MS are in the pontine region and result in the damage of primary afferent neurons while in some patients the neurovascular decompression may be the cause of damage(12). Although in some patients both mechanisms may be evident. It is considered that in MS T-cells activity is increased that causes

increased inflammatory changes in the plaques thus causing more ephaptic nerve conduction(13).

In patients with TN related to MS neuroimaging techniques and MRI are used for detecting plaques in the pathway of trigeminal nerve root. Trigeminal reflex testing has 90% sensitivity and specificity for knowing any impairment in trigeminal nerve. MRI is routinely used for diagnosing MS and TN related MS. MRI scans (T2 weighted) are helpful in identifying plaques in the pathway of trigeminal nerve root(14). The brainstem lesions associated with MS related TN are more scattered and can be found in the subnucleusoralis of the spinal complex of trigeminal nerve. Since MRI is helpful in assessing plaques trigeminal nerve root pathways, it also provides an insight vision to the neurovascular compression present in the root entry zone of trigeminal nerve. Literature reveals that morphological changes associated with trigeminal nerve such atrophy, flattening, dislocation were highly associated with symptoms of TN related with MS(15).

As far as the management of the condition under study is concerned, a number of strategies are used to control pain of TN related to MS that is from the use of injections (glycerol, alcohol) and antiepileptic drugs such carbamazepine, gabapentin, topiramte, lamotrigine, misoprostol or combination of these to surgical treatments that include peripheral lesions distal to the ganglion, stereotactic radiosurgery, microvascular decompression in the posterior fossa and gasserian ganglion percutaneous techniques(16-18). The outcome of the pharmacological treatment is better either used alone or in combination with other drugs, but there is less literature available to support the better outcome of the surgical procedures.(19)

The variable etiologies of trigeminal neuralgia associated with multiple sclerosis have stressed a need to perform neuroimaging procedures for timely investigation. Therefore, there was a need to conduct a study on role of MRI in finding association between trigeminal neuralgia with multiple sclerosis.

METHODOLOGY

The prospective cohort study was conducted for six months in Radiology Department of Hayatabad Medical Complex, Peshawar from September 2020 to February 2021. An ethical approval was taken from the research ethical review committee of the hospital. The informed consent was taken from patients, the data of the patients was kept confidential and purpose of the study was explained to them.

Study Participants: Initially 250 patients were screened for multiple sclerosis. The study a recruited a total of 35 patients of MS visited neuroradiology department, out of which 26 patients were enrolled in the study. The participants with age of 18 years and onward of both genders with definitive symptoms of TN with MS that is having unilateral TN pain (that is sharp shooting electric pulse like) lasting for up-to 2minutes precipitated with an environmental stimulus were included in the study. The patients (n=6) with bilateral MS with TN and cognitive disturbances (n=3) were excluded from the study. We also collected data from the participants coming to the neurology department with MS related trigeminal sensory disturbances (n=20) and classic trigeminal neuralgia patients(n=120).

Clinical Examination: The precise sensory clinical examination of patients was done by the piece of cotton and pinprick was done by wooden cocktail stick.

Trigeminal reflexes testing: Neurophysiological testing includes early and late blink reflex (R1 and R2) following electric supraorbital nerve stimulation and early and late masseter inhibitory (S1 and S2) after electric mental nerve stimulation. The electromyography (EMG) signals were recorded for both procedures and latency and duration of stimulation was observed.

The tests were considered abnormal with short latency periods or exceeded time period than normal ranges.

Study Variables: The study variables included age at onset of MS, gender, side of TN and affected division of trigeminal nerve.

MRI Investigations: All patients underwent MRI with 3T magnet having 12 channel head coil. The MRI protocols included 3D gradient recalled echo (GRE) T1 weighted image with repetition time(TR) of 2300ms, echo time(TE) of 2.98ms, inversion time of 900ms, flip angle of 9 degrees with field of view of 240x256 mm 208 slices 1mm isometric voxel on sagittal plane and turbo spin echo(TSE).T2 weighted image: TE 104ms, TR 6000ms, FOV 220mm , slice thickness 3mm and flip angle 150 degree.

These investigation protocols were helpful in diagnosing pontine demyelinating plaques in the pathway of trigeminal nerve root and were considered present when the lesion involved the intra-pontine segment of trigeminal nerve root.

Statistical Analysis: One-way ANOVA (analysis of variance) was used to compare difference in age at the onset of trigeminal neuralgia symptoms with multiple sclerosis, MS related sensory disturbances and classic TN. Gender and involved side frequency as well as association between demyelinating plaques and neurovascular compression was compared by using Fischer exact test. Goodness-fit X^2test was used to find that plaques were homogenously distributed on the affected side or not. Wilcoxon test was used to check the reflex variable between the affected and unaffected side.

RESULTS

The study recruited a total of 26 participants with MS related TN. The clinical examination didn't show any difference between the three groups with the p-value less than 0.001.Age at the onset of MS was younger in patients with MS related sensory disturbances compared to other two groups, with p-value less than 0.05. The frequency of the affected side was different in all three groups with the p-value less than 0.05 as tested by Fischer exact test (see table for details). The right side of the face was more affected than left side. Among 26 selected participants with MS related TN n=12 had sensory disturbances such as tactile sensation while n=14 had both sensory and pinprick disturbed sensations.

Trigeminal reflex tests done for different components such as R1 and SP1 showed longer latency periods for the affected side after stimulation and unaffected side after stimulation with the mean of 14.2± 4.4 and 15.3±3.2, 16.3±4.2 and 17.4±5.2ms and p-value less than 0.001 as shown by Wilcoxon test.

MRI showed demyelinating plaques in all participants on the affected side. Out of these 26 patients n=16 had neurovascular compression on trigeminal nerve side. No significant difference was found in the size of MS plaques present in the trigeminal nerve entry root with the mean of 1.6±0.8 versus 1.3±0.3 $mm^{2.}$ The frequency of neurovascular compression and association between neurovascular compression and demyelination plaques was higher on affected side with the p-value of 0.001, as shown by fisher exact test. Root entry zone plaques and neurovascular compressions were unevenly distributed on affected side as compared to the unaffected side with p-value less than 0.001 as assessed by X^2 test.

Out of these 26 patients n=21 were on medications, n=4 on injections and n=1 had undergone surgical procedure in patients with MS related to TN. In patients with MS related trigeminal sensory disturbances n=18 were on medications and n=2 were on injections. In patients with classic TN all n=148 patients were on medications. See table 2 for details.

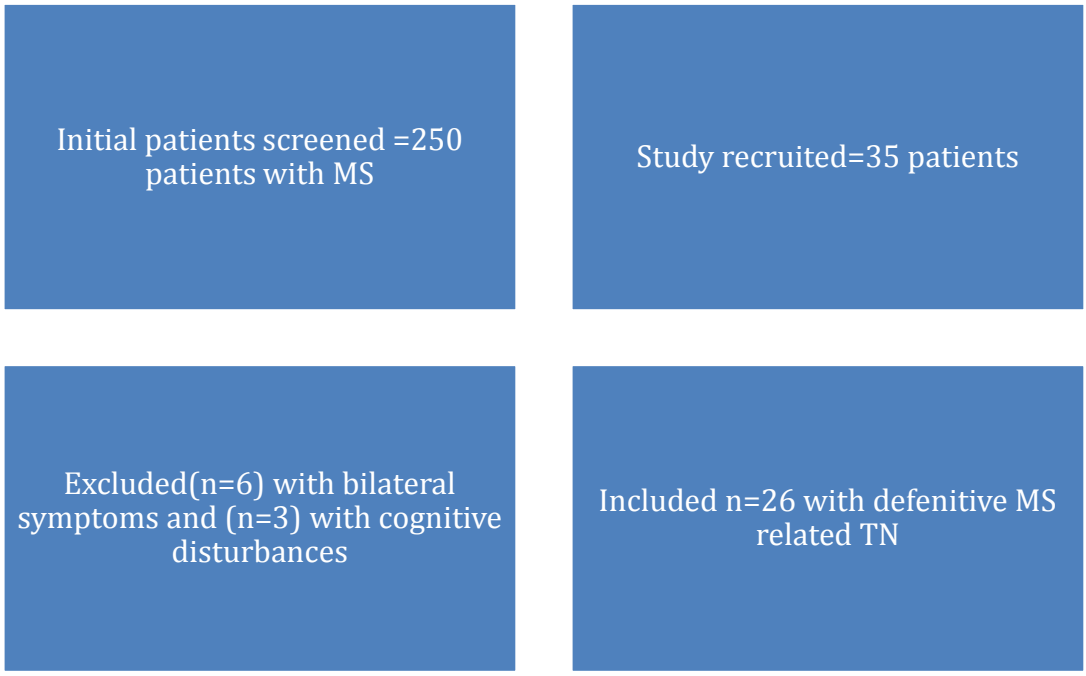

Table 1: Showing clinical examination in three different groups

Demographic data	MS related TN (n=26)	MS related trigeminal sensory disturbances(n=20)	Classic TN (n=120)	P-value (test)
Gender(M:F)	15:11	16:4	73:47	0.6 (Fischer exact test)
Age at the onset of MS	42.34±12.0	39.41±10.1	---	
Age at the onset of trigeminal symptoms	45±9.2	34±7.2	38.23±7.7	0.000(ANOVA)
TN side R:L	18:8	17:3	109:11	0.02 (Fischer exact test)

Table 2: Showing outcome of treatment strategies

Variable	MS related TN n=26(%)	MS with Trigeminal sensory disturbances n=20(%)	Classic TN n=120(%)	Outcome of treatment
Medication	21(80.76%)	18(90%)	120(100%)	Pain control
Injections	4(15.3%)	2(10%)	0	Pain control
Surgical intervention	1(3.8%)	0	0	Pain free

DISCUSSION

Studies shows that MRI is mostly used in diagnosing MS and identifying TN. In patients with TN secondary to MS the T2 weighted MRI scans helps in identification of the linear plaques in the ventrolateral pons which are located trigeminal root entry zone and the trigeminal nuclei thus MRI plays a crucial role in finding association between the two conditions(20).

The results of the current study showed that there was significant association between trigeminal neuralgia and multiple sclerosis as observed by MRI. The study findings suggest that in many patients with MS pontine plaques and neurovascular compression together causes TN through a process called inflammatory demyelination or double crush mechanism, which was only evident by using MRI-scans.

Some studies suggest that MRI can be a useful tool in investigating the anatomy and the vascular relationships of the trigeminal nerve. Moreover, it is also a useful tool in assessing neurovascular compression of the trigeminal nerve at the root entry zone. The neurovascular compression with morphological changes was highly

associated with the symptomatic side in TN related MS patients(21).

TN is caused by neurovascular compression which is widely used but is not universally accepted. The demonstration of vascular compression of the nerve root was not possible but the literature shows that MRI can include or exclude vascular compression of the nerve root and can be a good predicator that whether patients will get benefit from the microvascular decompression(12).

Though many advancements in both MRI and clinical technology took place but the diagnosis of MS remains clinical and most of the clinicians are reluctant to forward a diagnosis of MS with firm clinical evidence. Another study showed that in patients MS and TN caused by demyelinating plaque with intra axial primary afferents, the MRI investigation showed a significant relationship between symptomatic neurovascular compression and MS related TN.(22)

Some previous studies showed that a coexisting pontine demyelinating plaque and neurovascular compression and mostly exists in patients having MS related TN. This must prompt neurologists to screen such patients for neurovascular compression. In this regard, MRI reports confirming a symptomatic neurovascular compression can be useful in planning surgical treatment of patients concerned(23).

Almost all literature was in favor of using MRI as a choice of imaging technique to find the association between MS and TN and was helpful in timely treatment for patients.

CONCLUSION

The study showed significant association between trigeminal neuralgia and multiple sclerosis with the greater efficacy of using MRI as imaging technique to find this association.

Conflict of Interest: The authors declare no conflict of interest regarding the study.

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