CASE REPORT 3

Nerve vs musculoskeletal pain- a case of debilitating pain condition

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Introduction

According to the International Association of the Study of Pain (IASP), pain is identified as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" [(1)].

Pain is one of the most common reasons why patients seek medical attention, accounting up to 40% of cases visiting their physicians [(2)]. It is a significant global health problem with estimates of 20% of the adult population suffering from pain and 10% are diagnosed with chronic pain annually [(3)].

Chronic pain is defined as "pain that persists or recurs for more than 3 months". It is considered as a major source of suffering and can have significant impact on the quality of different aspects of patients' physical, psychological, and social life [(4, 5)]. Chronic pain has an estimated prevalence of 31% of studied population and this can be as high as 62% of people over the age of 75 years. There is a slight female predilection with female-male ratio of 1.2:1 [(6, 7)].

According to the International Classification of Headache Disorders 3rd edition (ICHD-3), glossopharyngeal neuralgia (GPN) is classified under *13. Painful lesions of the cranial nerves and other facial pain*, and it is described as : "*A disorder characterized by unilateral brief stabbing pain, abrupt in onset and termination, in the distributions not only of the glossopharyngeal nerve but also of the auricular and pharyngeal branches of the vagus nerve. Pain is experienced in the ear, base of the tongue, tonsillar fossa and/or beneath the angle of the jaw. It is commonly provoked by swallowing, talking or coughing and may remit and relapse in the fashion of trigeminal neuralgia*" [(8)].

The term glossopharyngeal neuralgia was first suggested by Harris in 1921, where he described a rare condition of symptoms mimicking those of trigeminal neuralgia but affecting different anatomical locations of throat, tonsillar and anterior pillar of fauces. He described this condition in two cases of a man aged 40 years and a woman aged 87 years [(9)].

The pain of GPN can be so severe that it stops the patient from eating and may lead to weight loss. Symptoms are characterised by unilateral severe short lasting stabbing or electric-shock like pain provoked by swallowing, taking, coughing or yawning along the distribution of the glossopharyngeal never and closely related branches of the vagus nerve (auricular and pharyngal) covering the anatomical areas of posterior tongue, pharynx and parapharyngeal areas, under mandibular angle, and ear [(10)]. There might be periods of relapses and remissions

as in trigeminal neuralgia. In 10% of patients, there are excessive vagal symptoms leading to bradycardia, hypotension, syncope, seizures or even cardiac arrest [11, 12].

ICHD-3 classifies GPN into three categories based on the underlying cause but sharing the characteristic symptoms [8]:

- Classical GPN with demonstrable neurovascular compression of the glossopharyngeal nerve root, either by MRI or surgery.
- Secondary GPN caused by underlying disease such as neck trauma, multiple sclerosis, tonsillar or regional tumours, or cerebellopontine angle tumours.
- Idiopathic GPN with no evidence either of neurovascular compression or underlying disease.

Incidence of GPN is estimated to be 0.7% per 100,000 of population per year [13], it has a slight female predilection with a F:M ratio of 1.3:1, average age of presentation of 61 years, and affects the left hand side more frequently [12].

Similar to other cranial neuralgias, the pathophysiology of idiopathic GPN remains poorly understood. The glossopharyngeal nerve, after leaving the medulla oblongata, passes laterally to exit the skull through the jugular foramen along with the vagus and accessory nerves, The glossopharyngeal nerve is responsible for multiple functions of general somatic sensation the (tympanic membrane, posterior tongue, and upper pharynx), visceral sensation (sensory information from the carotid sinus and carotid body), brachial motor innervation to the stylopharyngeus muscle, special visceral sensation (taste sensation from the posterior one-third of the tongue), and parasympathetic innervation of the parotid gland via the otic ganglion. The carotid branch of glossopharyngeal nerve communicates with the vagus nerve and receives information from the chemoreceptors in the carotid body and baroreceptors in the carotid sinus. Activation of this branch during GPN attack may activate the vagus nerve. This vagal activation may explain the cardiovascular consequences associated with GPN sometimes [11, 14].

Diagnosis of glossopharyngeal neuralgia is based on the clinical symptoms that need to be fulfilled according to the ICHD-3 diagnostic criteria *(Table1)*[8]. Investigations such as MRI or CT scans are helpful to rule out secondary cause of the disease and in planning for surgical management.

Pharmacological management remains the first line of management GPN. Depending on the clinical behaviour and symptomatology of the condition, the significance of the underlying disease (neurovascular compression, tumour, trauma), and extent of cardiovascular activation treatment can be medical, surgical, or combined [15].

Case Report

A 41-year old male was referred to the Oral Medicine Department of the Royal Dental Hospital of Melbourne by his primary care dentist with a complaint of severe sharp pain around the left angle of the mandible for the past week. Pain had been affecting the same area of left mandible for approximately 6 months and was investigated overseas, but the patient was not aware of any specific diagnosis or pathology. General dentist had ruled out odontogenic origin of pain. Patient was seen in December 2018, 3 weeks after the referral was received by our department.

The medical history was unremarkable except that the patient was on carbamazepine 400 mg twice daily prescribed by the overseas doctor to manage his current facial pain. Patient had been on the medication for 1 month, but this was of little help. Overseas MRI of the neck and face was unremarkable for pathology or underlying cause of pain.

In the social history, patient lives with his brother. He is married and has 3 children. His wife and children remained overseas since his return to Australia 6 months ago.

Dental history was significant for facial trauma and broken jaw 15 years ago, he had microplates and screws in the anterior left body of mandible. He had radiographic evidence of interproximal carious lesions in teeth 36, 37 which were noted by the general dentist and were asymptomatic and non-contributary to the patient's presenting complaint *(Fig.1)*.

Patient described pain of 6-month duration with a short period of remission while overseas. The pain starts from the left ear and goes down to the angle of mandible. In the previous month before the appointment, the pain was so severe and caused significant negative impact on patient's quality of life and had been affecting his ability to eat, drink, talk and sleep. Patient described a persistent background pain of 3-5/10 on Visual Analogue Scale (VAS) and this usually goes up to 10/10 during episodic attacks. Triggering factors could be disturbed sleep due to the nature of shift work as a taxi driver, sleeping on the left-hand side, wide mouth opening and yawning. The quality of pain was described as pressure and stretching type of pain, and it was most severe in the morning upon waking.

Extra-oral examination was within normal limits. There was no regional lymphadenopathy, swelling, or tenderness. TMJ and masticatory muscle examination revealed no familiar pain, functional limitation, or joint noises. Mouth opening was wide and straight. Intra-orally, there was no obvious clinical dental caries or odontogenic origin of pain, and the oral mucosa appeared healthy. There was mild left lateral pterygoid tenderness. Orthopantomogram and TMJ transcranial view did not show any obvious TMJ, maxillary, or mandibular osseous pathology *(Fig.1)*.

Our provisional diagnosis was that of possible *temporomandibular disorder (TMD) in the form of myofascial pain with referral* [16] *with considerable psychosocial component*. Education and counselling were provided on the day, with view to communicate with patient's physician for further medical management and investigations. Patient was booked for a review in 4 weeks.

As the patient was on 800 mg daily carbamazepine for a month with minimal relief, and as he did not have any baseline haematological assessment, a letter to his general practice doctor was sent detailing our provisional diagnosis, and requesting tapering down carbamazepine while trialling low dose amitriptyline which is known to provide analgesic effect in some patients with chronic pain conditions [17, 18]. The need for baseline full blood exam, liver function test, and blood biochemistry to monitor the effect of carbamazepine was highlighted in the letter.

Four weeks later, patient returned for a review. His laboratory investigations were all within normal limits. In coordination with his doctor, he started 25mg amitriptyline nocturnally and gradually decreased his carbamazepine to 200mg bid. This had resulted in a relapse of severe pain episodes, characterised by electric shock like pain attacks, lasting for 30 seconds, and triggered by talking and swallowing. These attacks were not reported in the previous visit and patient noted them more frequently after tapering down carbamazepine. During the consultation, patient experienced multiple electric shock like attacks affecting the left retromandibular area and the area under the left mandibular angle. The clinical exam was unremarkable in this visit and our working diagnosis was reconsidered to GPN. Patient was asked to gradually increase his carbamazepine dosage to 200mg four times daily, start pregabalin 25mg nocturnally and to cease amitriptyline. A request for brain MRI was given, and this has shown a prominent *left Posterior Inferior Cerebellar Artery (PICA) loop contacting and displacing the root entry zone of the cranial nerve IX-XI complex posteriorly (Fig.2)*.

Upon review 2 weeks later, patient reported 75% reduction in painful episodes, however he still experienced infrequent episodes with function. Consequently, Lyrica dose was titrated to 75 mg nocturnally while maintaining Tegretol at the same dose of 200mg QDS. Patient was reviewed a month later and he remained stable with manageable pain level. He saw a spinal neurosurgeon who reported that patient can be a good candidate for surgical procedure. But since the pain level was controlled by medication, the surgeon suggested to leave the surgical option as a second resort if pain recurs *(Fig.3)*. Patient has then been followed up and has been stable up to the last review in August 2019.

Discussion

Glossopharyngeal neuralgia (GPN) is not only an isolated painful condition that requires symptomatic management, in certain cases, it may be life-threatening as a result of associated cardiovascular consequences. The significance of vagal symptoms association with some GPN cases necessitates the need for a detailed history taking with focus on cardiac symptoms to identify patients at risk of serious events as a result of their GPN and manage them accordingly. Vagal symptoms can be present in approximately 10% of GPN patient and may be experienced as bradycardia, hypotension, syncope, seizures, and cardiac arrest in extreme cases [(19)]. In the presented case, patient did not report any of these symptoms in any of his reviews.

Diagnosis of GPN can be reached based on the clinical symptoms and following diagnostic criteria set by the ICHD-3 *(Table 1)* [(8)] .The diagnosis of classical or secondary GPN requires fulfilment of the criteria for idiopathic GPN and MRI demonstrating neurovascular compression of the glossopharyngeal nerve root or an underlying pathology respectively [(8)]. Secondary causes include neck trauma, multiple sclerosis, tonsillar or regional tumours, Paget's disease, cerebellopontine angle tumours, Eagle's syndrome, and Arnold–Chiari malformation [(20, 21)].

Other painful cranial neuralgias such as trigeminal, superior laryngeal, and nervus intermedius neuralgias may have overlapping symptoms with GPN and must be included in the differential diagnosis. Temporomandibular disorder (TMD) can also be listed in the differential diagnosis of GPN as the anatomical distribution of pain symptoms in both conditions may overlap. GPN and trigeminal neuralgia are both cranial neuralgias with similar pathophysiology and although the location of pain is clearly different, it is possible for the two conditions to coexist [(19, 20)].

Management of GPN is similar to that of trigeminal neuralgia, being primarily medical. Anticonvulsant agents such as carbamazepine or oxcarbazepine, are the drugs of choice [22, 23]. Carbamazepine can result in significant pain reduction, reduction of frequency of paroxysms and effective suppression of syncope and related cardiac events [24, 25]. If carbamazepine is not effective or intolerable, second line medications such as phenytoin, lamotrigine, gabapentin, or pregabalin can be used as an add on or replacement therapy [26].

If considerable cardiovascular symptoms are associated with painful episodes, or still present after controlling pain symptoms with anticonvulsant medications, administration of atropine can be considered to prevent the possible life-threatening cardiac events [11, 23].

In case of GPN refractory to pharmacological treatment, the degree of disability and presence of significant cardiovascular event associated with GPN dictates further management protocols. Surgical intervention in the form of microvascular decompression (MVD) is safe, effective, and promising second-line treatment and is reserved for cases of failed medical management or if the treatment is not tolerated [27]. MVD provides total pain relief for long term in the great majority of patients (80%-90%) with no need for continuation of anticonvulsant therapy after surgery [26, 28] , this is particularly predictable in cases of classical GPN with MRI confirmed neurovascular compression [23, 29].The surgery is associated with insignificant side effects , mainly in the form of transient cranial nerve deficit with difficulties in swallowing or vocal cord paresis [29].

If MVD is technically difficult, other neurosurgical options can be considered. Percutaneous radiofrequency rhizotomy and direct surgical resection are options that can be considered for patients who have no evidence of neurovascular compression, those who are not suitable for MVD, or had no success with MVD. Those procedures are usually associated with a higher recurrence rate when compared to MVD [20]. Stereotactic radiosurgery with gamma knife targeting the glossopharyngeal nerve at the jugular foramen level is a well-tolerated treatment with no acute or long term complications [30].

References

1. Treede RD. The International Association for the Study of Pain definition of pain: as valid in 2018 as in 1979, but in need of regularly updated footnotes. Pain reports. 2018;3(2):e643.
2. Mantyselka P, Kumpusalo E, Ahonen R, Kumpusalo A, Kauhanen J, Viinamaki H, et al. Pain as a reason to visit the doctor: a study in Finnish primary health care. Pain. 2001;89(2-3):175-80.
3. Goldberg DS, McGee SJ. Pain as a global public health priority. BMC public health. 2011;11:770.
4. Treede R-D, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain. 2019;160(1):19-27.
5. Dueñas M, Ojeda B, Salazar A, Mico JA, Failde I. A review of chronic pain impact on patients, their social environment and the health care system. Journal of pain research. 2016;9:457-67.
6. Fayaz A, Croft P, Langford RM, Donaldson LJ, Jones GT. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. BMJ Open. 2016;6(6):e010364.
7. Steingrímsdóttir ÓA, Landmark T, Macfarlane GJ, Nielsen CS. Defining chronic pain in epidemiological studies: a systematic review and meta-analysis. Pain. 2017;158(11):2092-107.
8. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38(1):1-211.
9. Harris W. PERSISTENT PAIN IN LESIONS OF THE PERIPHERAL AND CENTRAL NERVOUS SYSTEM. British medical journal. 1921;2(3178):896-900.
10. O'Neill F, Nurmikko T, Sommer C. Other facial neuralgias. Cephalalgia. 2017;37(7):658-69.
11. Blumenfeld A, Nikolskaya G. Glossopharyngeal neuralgia. Current pain and headache reports. 2013;17(7):343.
12. Martínez-González JM, Martínez-Rodríguez N, Calvo-Guirado JL, Brinkmann JC-B, Dorado CB. Glossopharyngeal Neuralgia: A Presentation of 14 Cases. Journal of Oral and Maxillofacial Surgery. 2011;69(6):e38-e41.
13. Katusic S, Williams DB, Beard CM, Bergstralh E, Kurland LT. Incidence and Clinical Features of Glossopharyngeal Neuralgia, Rochester, Minnesota, 1945–1984. Neuroepidemiology. 1991;10(5-6):266-75.
14. Shah RJ PD. Glossopharyngeal Neuralgia.2019 [Updated 2019 May 10].
15. Ma Y, Li YF, Wang QC, Wang B, Huang HT. Neurosurgical treatment of glossopharyngeal neuralgia: analysis of 103 cases. Journal of neurosurgery. 2016;124(4):1088-92.
16. Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet JP, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Group†. Journal of oral & facial pain and headache. 2014;28(1):6-27.
17. List T, Jensen RH. Temporomandibular disorders: Old ideas and new concepts. Cephalalgia. 2017;37(7):692-704.
18. Hersh EV, Balasubramaniam R, Pinto A. Pharmacologic management of temporomandibular disorders. Oral and maxillofacial surgery clinics of North America. 2008;20(2):197-210, vi.
19. Bruyn GW. Glossopharyngeal Neuralgia. Cephalalgia. 1983;3(3):143-57.
20. Teixeira MJ, de Siqueira SR, Bor-Seng-Shu E. Glossopharyngeal neuralgia: neurosurgical treatment and differential diagnosis. Acta Neurochir (Wien). 2008;150(5):471-5; discussion 5.
21. Pearce JM. Glossopharyngeal neuralgia. European neurology. 2006;55(1):49-52.
22. Bendtsen L, Zakrzewska JM, Abbott J, Braschinsky M, Di Stefano G, Donnet A, et al. European Academy of Neurology guideline on trigeminal neuralgia. European journal of neurology. 2019;26(6):831-49.
23. Franzini A, Messina G, Franzini A, Marchetti M, Ferroli P, Fariselli L, et al. Treatments of glossopharyngeal neuralgia: towards standard procedures. Neurological Sciences. 2017;38(1):51-5.
24. den Hartog AW, Jansen E, Kal JE, Duyndam D, Visser J, van den Munckhof P, et al. Recurrent syncope due to glossopharyngeal neuralgia. HeartRhythm Case Reports. 2017;3(1):73-7.
25. Saviolo R, Fiasconaro G. Treatment of glossopharyngeal neuralgia by carbamazepine. British heart journal. 1987;58(3):291-2.
26. Chen J, Sindou M. Vago-glossopharyngeal neuralgia: a literature review of neurosurgical experience. Acta Neurochirurgica. 2015;157(2):311-21.
27. Patel A, Kassam A, Horowitz M, Chang YF. Microvascular decompression in the management of glossopharyngeal neuralgia: analysis of 217 cases. Neurosurgery. 2002;50(4):705-10; discussion 10-1.
28. Kim MK, Park JS, Ahn YH. Microvascular Decompression for Glossopharyngeal Neuralgia: Clinical Analyses of 30 Cases. Journal of Korean Neurosurgical Society. 2017;60(6):738-48.
29. Gaul C, Hastreiter P, Duncker A, Naraghi R. Diagnosis and neurosurgical treatment of glossopharyngeal neuralgia: clinical findings and 3-D visualization of neurovascular compression in 19 consecutive patients. The journal of headache and pain. 2011;12(5):527-34.
30. O'Connor JK, Bidiwala S. Effectiveness and safety of Gamma Knife radiosurgery for glossopharyngeal neuralgia. Proceedings (Baylor University Medical Center). 2013;26(3):262-4.

Table 1 ICHD-3 Diagnostic criteria for GPN [8]:

A. Recurring paroxysmal attacks of unilateral pain in the distribution of the glossopharyngeal nerve[1]

and fulfilling criterion B

B. Pain has all of the following characteristics:

1. lasting from a few seconds to two minutes
2. severe intensity
3. electric shock-like, shooting, stabbing or sharp in quality
4. precipitated by swallowing, coughing, talking or yawning

C. Not better accounted for by another ICHD-3 diagnosis.

1. Within the posterior part of the tongue, tonsillar fossa, pharynx or angle of the lower jaw and/or in the ear.

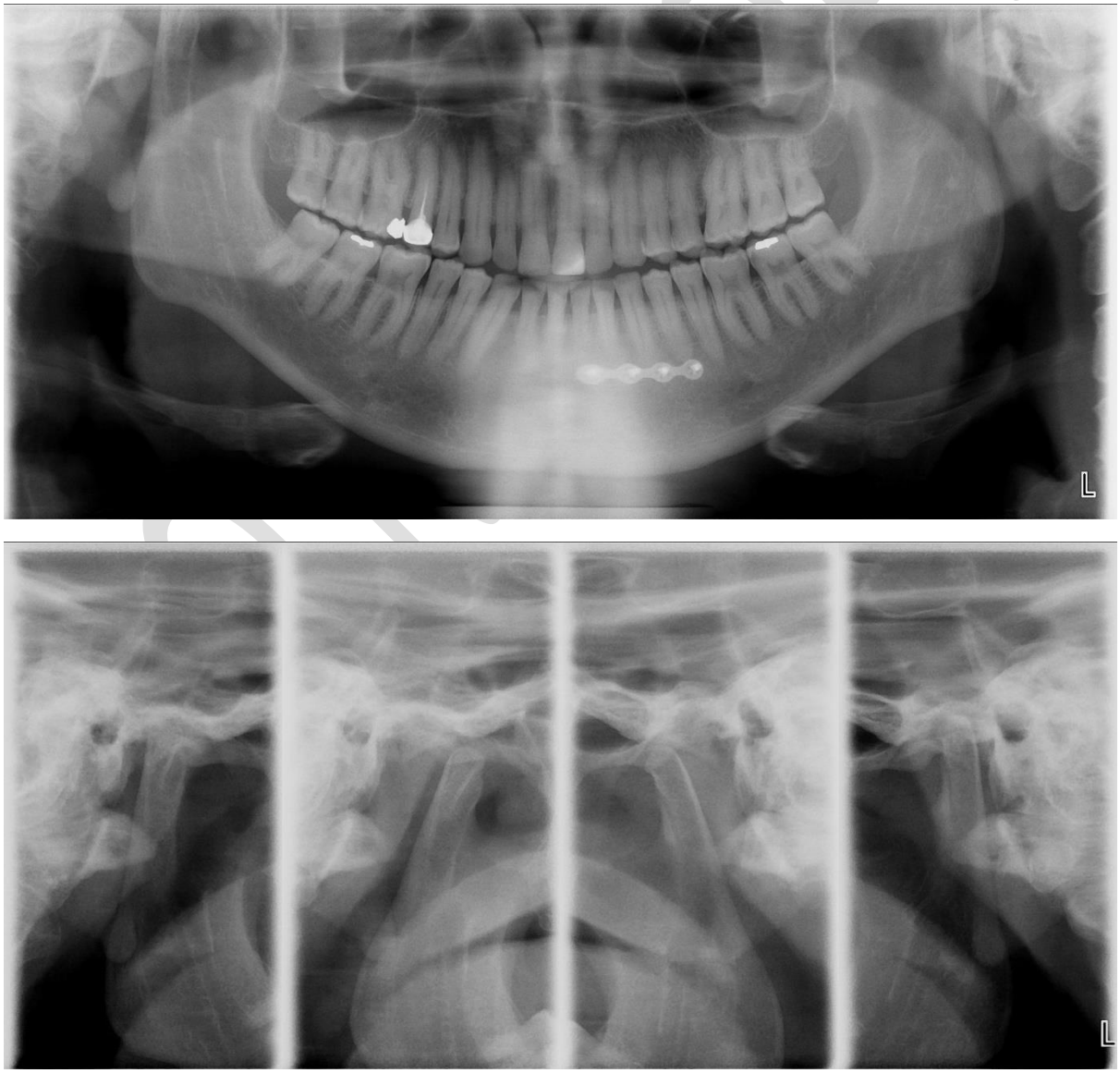
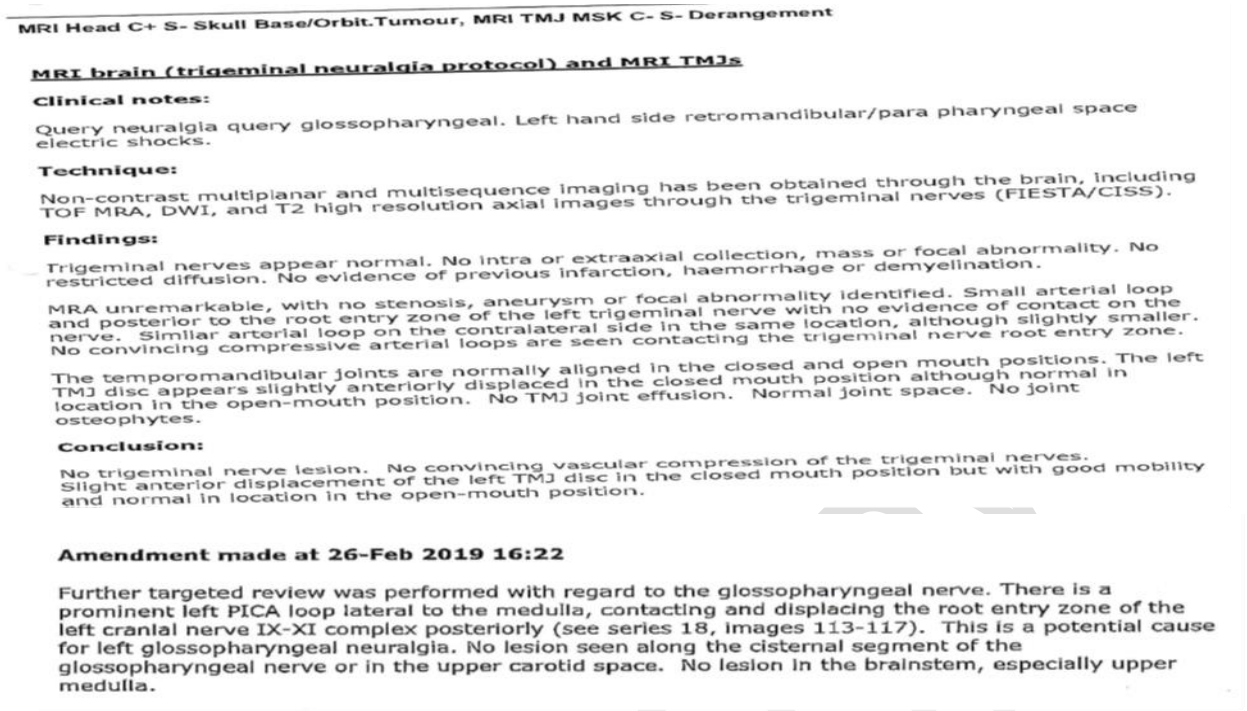


Figure 1: OPG and transcranial TMJ view . Interproximal carious lesions 36,37 noted, and a microplate in the left body of mandible. Although there is a sign of left condylar neck thinning, this was clinically irreleavant.



MRI Head C+ S- Skull Base/Orbit.Tumour, MRI TMJ MSK C- S- Derangement

MRI brain (trigeminal neuralgia protocol) and MRI TMJs

Clinical notes:

Query neuralgia query glossopharyngeal. Left hand side retromandibular/para pharyngeal space electric shocks.

Technique:

Non-contrast multiplanar and multisequence imaging has been obtained through the brain, including TOF MRA, DWI, and T2 high resolution axial images through the trigeminal nerves (FIESTA/CISS).

Findings:

Trigeminal nerves appear normal. No intra or extraaxial collection, mass or focal abnormality. No restricted diffusion. No evidence of previous infarction, haemorrhage or demyelination.

MRA unremarkable, with no stenosis, aneurysm or focal abnormality identified. Small arterial loop and posterior to the root entry zone of the left trigeminal nerve with no evidence of contact on the nerve. Similar arterial loop on the contralateral side in the same location, although slightly smaller. No convincing compressive arterial loops are seen contacting the trigeminal nerve root entry zone.

The temporomandibular joints are normally aligned in the closed and open mouth positions. The left TMJ disc appears slightly anteriorly displaced in the closed mouth position although normal in location in the open-mouth position. No TMJ joint effusion. Normal joint space. No joint osteophytes.

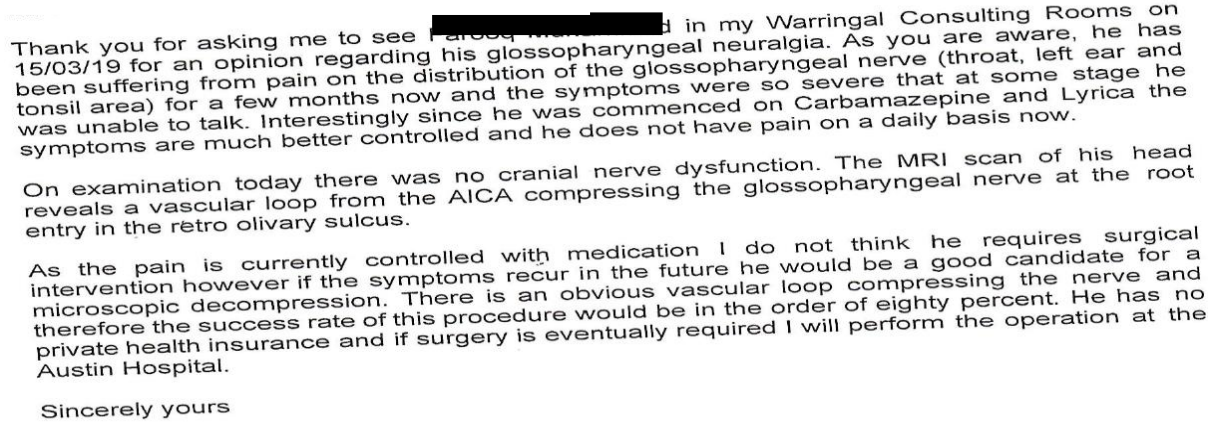
Conclusion:

No trigeminal nerve lesion. No convincing vascular compression of the trigeminal nerves. Slight anterior displacement of the left TMJ disc in the closed mouth position but with good mobility and normal in location in the open-mouth position.

Amendment made at 26-Feb 2019 16:22

Further targeted review was performed with regard to the glossopharyngeal nerve. There is a prominent left PICA loop lateral to the medulla, contacting and displacing the root entry zone of the left cranial nerve IX-XI complex posteriorly (see series 18, images 113-117). This is a potential cause for left glossopharyngeal neuralgia. No lesion seen along the cisternal segment of the glossopharyngeal nerve or in the upper carotid space. No lesion in the brainstem, especially upper medulla.

Figure 2. MRI report. Initially reported in regard to trigeminal nerve, although the request was specific for glossopharyngeal nerve. A follow up call to the radiologist resulted in review of the imaging and amendment of the report as above.



Thank you for asking me to see [redacted] in my Warringal Consulting Rooms on 15/03/19 for an opinion regarding his glossopharyngeal neuralgia. As you are aware, he has been suffering from pain on the distribution of the glossopharyngeal nerve (throat, left ear and tonsil area) for a few months now and the symptoms were so severe that at some stage he was unable to talk. Interestingly since he was commenced on Carbamazepine and Lyrica the symptoms are much better controlled and he does not have pain on a daily basis now.

On examination today there was no cranial nerve dysfunction. The MRI scan of his head reveals a vascular loop from the AICA compressing the glossopharyngeal nerve at the root entry in the retro olivary sulcus.

As the pain is currently controlled with medication I do not think he requires surgical intervention however if the symptoms recur in the future he would be a good candidate for a microscopic decompression. There is an obvious vascular loop compressing the nerve and therefore the success rate of this procedure would be in the order of eighty percent. He has no private health insurance and if surgery is eventually required I will perform the operation at the Austin Hospital.

Sincerely yours

Figure 3. Correspondence from Neuro/spinal surgeon.