Trigeminocardiac Reflex Elicited in the Head and Neck Region - A Case Report Triggered by the Removal of Jackson-Pratt Drain

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October 1, 2020

Abstract

Trigeminocardiac reflex (TCR) is a complex neurophysiological reflex manifesting acute or chronic hemodynamic perturbations. Neurosurgical triggers have been described extensively as the common cause of TCR. Variability of TCR manifestation mainly depend on the stimulant location. We present the first reported TCR that is triggered by removal of Jackson-Pratt drain.

Trigeminocardiac Reflex Elicited by Removal of A Jackson-Pratt Drain

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Keywords: Trigeminocardiac reflex, bradycardia, auriculotemporal nerve

Key Clinical Message:

TCR may be life threatening, apart from surgical or traumatic triggers, TCR may occur even to a gentle stimulation. It is crucial to position a drain catheter away from the adjacent nerve fibers or any potential trigger point.

Introduction

Trigeminocardiac reflex (TCR) is a usually benign physiological phenomenon that triggered by a stimulus at any point along the trigeminal nerve or fifth cranial nerve (CN V). Exaggerated response to cause severe morbidity has been reported.

This phenomenon has not originally recognized as TCR, the nomenclature was formulated and revised after a long process over a century. In 1870, Florian Kratschmer first described cardiac arrhythmias after upper airway stimulation in cats and rabbits. This clinical observation has been known as Kratschmer reflex (KR).[1, 2] Giuseppe Dagnini published an Italian report in June 1908, regarding decreased heart rate while exerting direct pressure to the globe. Coincidently, in October 1908, Bernhard Aschner also reported a similar reflex in German literature.[3] Thereafter, it was often known as the Aschner phenomenon although Dagini

reflex or Dagini-Aschner reflex should be more appropriate according to the dates of the publication order. But the term oculocardiac reflex (OCR) was more widely used in later years with regards to associated reflex induced by stimulation of orbital or periorbital structures.[4] In 1969, Blanc did studies on dogs and reported that the stimulation on nasal mucosa can also induces cardiac response like bradypnea, bradycardia, and hypotension.[4, 5] In 1977, Kumada et al. reported a so-called trigeminal depressor response (TDR) during electrical stimulation within discrete sites of the trigeminal complex in anesthetized or decerebrated rabbits.[6] That publication suggested that autonomic reflex responses are elicited by both peripheral stimulation and central parts of the trigeminal pathway.[7] Other pioneers in this field include Anderson who described the blepharocardiac reflex in 1978,[8] Loewinger et al. proposed the equivalence of trigeminovagal reflex (TVR) and OCR.[9] Anesthetists Shelly and Church coined the term trigeminocardiac reflex (TCR) in 1988, suggesting that OCR is a subtype of TCR.[10]

In 1999, Schaller et al. first described the central TCR in humans during cerebellopontine angle and brainstem surgery.[11]The peripheral subtype of TCR had not been established until Schaller et al. developed the definition and classification of TCR in 2008.[12]

Owing to the cardiovascular alterations and the possible risk of tragic complications resulted from the TCR events, it is essential to have a comprehensive understanding on the mechanism, pathophysiology, predisposing risk factors, manifestations, diagnostic criteria, and prompt management of the TCR.

TCR occurrence has been reported during several neurosurgical procedures. But according to Schaller, TCR may also occur in 10%-18% of the maxillofacial, skull base and ophthalmic surgery.[13] Hereby we present a case to highlight the imperatives of TCR that is not restrained to an intraoperative period, but may also be triggered upon the minor stimulation postoperatively, such as removal of a drain around the branches of trigeminal nerve, as well as to review the prior literature addressing this phenomenon.

Case Report

A 53-year-old male patient (weighed 72.5 kg and height 167 cm) with unremarkable medical history had the habit of cigarette smoking (half a pack a day) for more than 20 years. He had a painful swelling on the left face, which was getting larger in the past six months. Head and neck computer tomography (CT) revealed a 2.6 x 2.7 x 3.2 cm^3 well-defined mass with heterogeneous enhancement in left parotid gland, suggesting benign tumor such as Warthin tumor or pleomorphic adenoma.

The patient received left superficial parotidectomy after having all negative results from routine clinical studies, including chest radiography, electrocardiography (Figure 1) and laboratory tests. He was classified as ASA II after the evaluation by anesthesiologist.

His baseline blood pressure (BP) and heart rate (HR) were 135/87 mmHg and 92 beats per min (bpm), respectively. The anesthetic agent included intravenous injection of propofol (100 mg), 2% lidocaine (50 mg), fentanyl (150 μg), and dexamethasone (5 mg). Right nasoetracheal intubation was facilitated by premedication with rocuronium (60 mg). The anesthesia was maintained with desflurane and oxygen, and controlled ventilation.

During surgical procedures, patient had stable HR and BP at 70-90 bpm and 90/50 - 140/85 mmHg, respectively. He had the left superficial parotidectomy with preservation of facial nerve, through an intra-operative monitoring with a nerve stimulator. A 10-French gauge (Fr) Jackson-Pratt (J-P) drain was placed before wound closure, and the entire surgical procedures were completed in 5.5 hours.

After the patient went through a smooth recovery of clinical course on a regular ward, the J-P drain was removed on the third post-operative day as the drainage fluid amount was decreased to 10 mL/day. His vital signs before the procedure were HR 73 bpm, BP 123/76 mmHg, respiratory rate 16 breathes per min.

Immediately after the removal of the J-P drain, the patient had transient consciousness change, and a delayed response with slurred speech. His heart rate was dropped to 48 bpm and blood pressure 125/81 mmHg. His level of consciousness was returned to normal within five minutes, without any signs of respiratory distress.

The 12-lead electrocardiogram (Figure 2) revealed sinus bradycardia at 50 bpm. We ordered laboratory examinations to rule out any other systemic or cardiogenic etiology.

The patient had negative laboratory test findings, including those of serum cardiac enzymes, serum electrolytes, and other blood common biochemical paramaters. He received no further intervention other than close monitoring because he had been asymptomatic.

In the following hours, the patient had no discomfort or complaint. His rechecked HR and BP were 71 bpm and 120/75 mmHg, respectively. Without having any untoward events, he was discharged two days later in stable general condition.

Discussion

Definition

Schaller first defined TCR as the sudden onset of parasympathetic dysrhythmia, sympathetic hypotension, apnea or gastric hypermobility during stimulation at any parts along the course of trigeminal nerve.[14] Nonetheless, the definition of TCR remains arbitrary and has no uniformity among all studies. Bosomworth et al. described that a positive reflex when HR is reduced to 10% or more.[15] While Schaller et al. defined the TCR when HR is reduced to less than 60 bpm accompanied with decreased MABP of 20% or more.[11] But according to Bailey, the TCR differs in individuals, and influenced by times, degree of pressure, posture, emotional state as well as physical condition, even in the same individual.[16] Anatomical location of stimulation plays an critical role on MABP perturbation, an increase or decrease of MABP is only facultative, so the criteria should not be limited to a certain percentage to define a TCR.[17]

According to two clinical trials done by Bohluli et al., the incidence of bradycardia differs between bilateral sagittal ramus split and Le Fort I osteotomies.[18, 19] Based on those findings, Sadr-Eshkevari et al. proposed that the cutoff point is 20% or more decreased HR for a definitive TCR. This cutoff point has been advocated to be reasonable in statistical and research aspects.[20] Furthermore, it can be incorporated as a true reflex while excluding other false positive cases.[21] Contrariwise, more diverse TCR-related episodes such as subtle changes less than 20% or even increased hemodynamic changes especially in those beyond central stimulation have been reported.[22-25] Therefore, some investigators found that the strict cutoff point of 20% is not longer suitable for all subtypes of TCR, suggesting an underestimate of the true incidence of TCR.[17]

Sadr-Eshkevari et al. suggested that the nomenclature has been misleading, because TCR has only been linked to cardiovascular changes caused by trigeminal stimulation. In fact, TCR was initially coined to represent definite autonomic changes due to stimulating the trigeminal nerve.[21] Some studies have used the term trigeminovagal reflex (TVR) since trigeminal and vagus nerves are the afferent and efferent pathways to form the reflex circuit.[26] TVR has been proposed to describe any other sudden autonomic response with or without hemodynamic changes on stimulating trigeminal nerve or its branches.[27, 28]

On the basis of the cause–effect relationship, Meuwly et al. introduced tw major and two minor criteria to identify the TCR. Major criteria are plausibility and reversibility, whereas minor criteria are repetition and prevention (Table 1).[27] The investigators insisted that a TCR event should attain those criteria, but not all of them must always be present to validate a TCR. Still, the more criteria are fulfilled, the better TCR is confirmed.[17, 27, 29]

Plausibility is referred to direct response to a physical or chemical stimulation on trigeminal nerve pathway, and existence of a time lag up to five seconds to prove a positive cause-effect relationship.[27] Reversibility indicates that the withdrawal of stimulus should cause abolishment of the TCR episode.[20, 29] Notwithstanding, continuing asystole that requires cardiopulmonary resuscitation despite ceasing of stimulation has also been reported, being addressed as a “point of no return” phenomenon.[30] For the minor criteria, repetition cannot ethically be tested, but recurrence of reflex is observed under some circumstances.[31] The prevention of TCR can be achieved through a delicate manipulation at the site of trigeminal nerve or its branches.[17] But it does not represent an absolute criteria from clinical and pathophysiological viewpoint.[27]

Back to the fundamental of definition, TCR should be a response of a physical or chemical stimulation on any sites of the course of trigeminal nerve, and pain reaction has to be excluded.[20, 32, 33] In our reported case, the patient had the event during the process of removing the J-P drain was transitory and without any pain. His HR during the episode was 30% lower than the baseline, which is compatible with the definitive criteria (> 20% difference) that apply to determine a TCR.

Considering the different subtypes of TCR, recent studies have worked on more practical definition to adapt with all types of TCR.[34, 35] In summary, the aforementioned definition of 20% changes in HR and MABP by Schaller et al. may still be reasonable for the central subtype, but the peripheral subtypes do not constantly elicit a decreased MABP, thus changes in MABP to define a TCR should be revised.[12] Further details would be addressed in the following discussion.

Anatomical pathways and pathophysiology

The trigeminal nerve is the largest cranial nerves and has two main components, sensory component (portio major) and motor root (portio minor). It travels from the posterior cranial fossa, passing through the trigeminal foramen to Meckel cave in the middle cranial fossa, where it forms the trigeminal Gasserian or semilunar ganglion and divides into three main divisions, ophthalmic division (V_1), maxillary division (V_2), and mandibular division (V_3). Ophthalmic nerve continues to travel within the superior orbital canal, maxillary nerve exits through the foramen rotundum, while mandibular nerve passes through the foramen ovale.

In animals, about two thirds of the sensory trigeminal nerve are composed of unmyelinated C-fibers, whereas the majority of myelinated fibers are small in diameter and involved in nociceptive pathway. Microneurographic studies revealed that activation of a single C-fiber or Aδ-fiber gives rise to a burning or stinging sensation. Tooth pulp that is innervated by large diameter Aβ-myelinated axons, whose conduction velocities from peripheral site to the Gasserian ganglion can already be as fast as 58 to 62 m/s in cats, in addition to the small diameter Aδ-fibers and C-fibers that have a faster conduction rate. The inputs from the trigeminal nerve activate the sensory trigeminal complex almost simultaneously.[14]

Figure 3 illustrates the reflex arc of TCR. In general, stimulation on the sensory nerve endings of the trigeminal nerve initiates the afferent arc by sending the sensory signals through the Gasserian ganglion to the trigeminal sensory nucleus within the vicinity of the floor of the 4th ventricle. The glutamatergic second-order neurons receive this sensory information, that are mostly lateral and slightly dorsal to the nucleus ambiguus in the ventral trigeminal nucleus.[14] The afferent pathway continues from the ventral trigeminal nucleus through the short internuncial nerve fibres in the reticular formation in brainstem to finally synapse on efferent cholinergic premotor parasympathetic cardioinhibitory neurones in the nucleus ambiguous and the dorsal motor nucleus of vagus. Activation of these parasympathetic cardioinhibitory vagal neurons terminate in the myocardium through the cardiac depressor nerves, to initiate the negative chronotropic and inotropic responses.[35, 36]

The pathophysiological pathway of the TCR has been studied extensively, marked differences between the central and peripheral subtypes have been noticed in regard to their afferent pathway and involved brainstem nuclei, resulting in different reflex arches. Coactivation of sympathetic and parasympathetic activities is weaker in the peripheral subtype than the central subtype. The peripherally stimulated TCR is relayed primarily through the spinal nucleus of trigeminal nerve, and onto the Kölliker-Fuse nucleus within the dorsolateral pons to regulate the respiratory rhythm. In contrast, the centrally stimulated TCR is conveyed through the short internuncial nerve fibers in the reticular formation within brainstem, then synapse on efferent premotor parasympathetic cardioinhibitory neurons in the nucleus ambiguus.[36]

TCR has also been hypothesized as a neurophysiological endogenous protective effect, which referred to as "oxygen-conserving reflexes" by Wolf et. al.[37] To protect the brain from any hypoxic insults, a high-energy and differentiated activation causes bradycardia (parasympathetic response), vasoconstriction, and increased blood pressure (sympathetic response), the oxygen is thus preserved during apnea.[4, 38] According to the experimental findings done by Schaller et al., TCR represents a central neurogenic reflex that generates

excitation of oxygen-sensitive neurons in the rostral ventrolateral medulla oblongata (RVLM), leading to rapid cerebrovascular vasodilatation that alters systemic and cerebral circulations, to divert blood to the brain or to increase blood flow within it.[14, 39] Furthermore, animal studies by Stephenson et. al. showed that no regional reductions in cerebral blood flow during TCR is not seen, but that heart rate, arterial blood gas tensions, and arterial pH are different in animals with TCR.[40, 41]

According to the route of the JP drain placed in our patient, auriculotemprotal nerve branches off from the mandibular division of trigeminal nerve was triggered when the drainage catheter was removed. This particular TCR phenomenon in our patient is the characteristic of peripheral subgroup of TCR, weak coactivation of sympathetic and parasympathetic activities causes bradycardia without remarkable hypotension, transient conscious change but without collapsing may be due to successfully preserved cerebral blood flow. Nevertheless, position of the drain catheter is a worthwhile consideration before closing the surgical wound (Figure 4). Classification and clinical manifestations

The TCR has been generally classified on the basis of the trigger location with respect to the Gasserian ganglion. Central or proximal TCR is incited by intracranial stimulation of the trigeminal nerve, proximal to the Gasserian ganglion. Peripheral or distal TCR is triggered by any extracranial stimulation along the course of trigeminal nerve, distal to the Gasserian ganglion. The peripheral TCR is further divided based on the affected branch of trigeminal nerve, the oculocardiac reflex (OCR, V_1) and the maxilla–mandibulocardiac reflex (MCR, V_2 -V_3). TCR triggered directly at the Gasserian ganglion itself is categorized as a separate subgroup, the Gasserian ganglion reflex (GGR).[22] Diving reflex (DR) is the most powerful autonomic reflex in humans that has also been classified as another independent subgroup of TCR.[14]To our understanding on the rationale of classification, DR produces similar reflex through introducing cold water or chemical stimuli onto nasal mucosa, where innervated by fine branches of trigeminal nerve,[20] it should thus be grouped as one of the subtypes of peripheral TCR. Moreover, although rare but a brainstem reflex (BR) subgroup has been introduced on the report of animal studies and clinical findings in brain trauma.[20]

Different variants of the TCR exhibit different characteristics and clinical manifestation (Figure 5). Apnea and gastric hypermobility are commonly seen in all the TCR subtypes. Decrease in HR is identical presented in both peripheral and central subtypes, however, a decreased MABP is always noticed in the central TCR and is considered necessary to the definition, but a change in MABP is facultative and is not always observed in the peripheral TCR.[20] Studies revealed that the physiological reactions in the peripheral TCR have greater variation than the central TCR. Clinical presentation such as bradycardia, bradycardia with simultaneous shortening of electrocardiogram QT interval, or bradycardia with apnea but increase in MABP, may be possibly observed in peripheral TCR. In contrast to the central TCR, profound activation of the cardiac vagal branch and distinct inhibition of the inferior cardiac sympathetic nerve[5] often result in bradycardia accompanied with hypotension.[36]

The OCR subtype of the peripheral TCR is usually associated with cardiodepressive effects,[7] particularly bradycardia with no hypotension.[42] Where the MCR subtype shows predominantly vagal responses, manifests with bradycardia and slight hypotension or normotension.[36] The phenomenon in our reported case is consistent with the MCR subtype of peripheral TCR, exhibiting bradycardia and normotension, on top of transient consciousness change.

Apart from bradycardia and apnea,[22] the main physiological difference between OCR, MCR and DR lies on MABP changes, whereby OCR and MCR usually elicited normotension or hypotension, while DR often causes hypertension due to peripheral vasoconstriction.[39]

Gasserian ganglion has a complex composition of parasympathetic and sympathetic fibers, thus the GGR subtype does not have a uniform characteristic, as the balance between the parasympathetic and sympathetic nerve system differs in each episode.[27] It may presents as pressor response such as tachycardia, extrasystole, hypertension, or depressor symptoms such as hypotension and bradycardia.[20]

The aforementioned differences among all of the TCR subtypes may be explained by the independent function of various affected receptors and variable influences from other coexisting pathways. Besides, the degree

of coactivation of sympathetic stimulation in theses subtypes does play a role. For example, sympathetic co-stimulation is substantial in peripheral subgroup, thus hypertension and tachycardia are more likely produced. Whereas such co-stimulation may be minimal in the central subtype, mostly lead to hypotension and bradycardia, depending on whether there is more post- or preganglionic stimulation.[20]

Apart from the classification based on trigger location, TCR is also presented as acute or chronic forms in accordance to the time of onset. Most of the clinically observed and reported TCR are acute onset and last for a short duration.[11] Nevertheless, a few of the chronic form of TCR have been reported, primarily related to OCR.[38, 43-45] The reported symptoms perseverance in chronic TCR range from days to months, the longest time to onset was reported by Yang et. al.,[43] an intraorbital foreign body that causes chronic OCR with a delayed diagnosis for 40 years. Permanent stimulation of the trigeminal nerve will lead to considerable deficits, and researchers assumed that there is substantial under-diagnosed cases of chronic TCR, including some postoperative complications might literally related to the TCR.[35]

Risk factors

As opposed to the TCR in the patient of our case, the reflex was stimulated through removing a JP drain three days after left superficial parotidectomy. But nearly all of the TCR reported to date is predominantly elicited intra-operatively or right after a traumatic event. Predisposing factors of intraoperative TCR consist of hypercapnia, hypoxemia, light general anesthesia, young age as children have a higher resting vagal tone, and strong or long-lasting provoking stimulus.[35]

The nature of the stimulus is the most important risk factor, which can be divided into mechanical, chemical, or electrical stimulation. Mechanical stretch is the most powerful stimulant, whereas sudden and sustained traction is more reflexogenic than smooth and gentle traction. Moreover, stimulation of bilateral trigeminal nerve fibers or the innervated structures tend to induce a more profound reflex than unilateral stimulation.[5] Nonetheless, a mild traction of scalp during skin closure has also been reported to induce TCR and even manifested as transient asystole.[46] Other reported mechanical stimulants include needle insertion, balloon inflation of the trigeminal ganglion, tumor resection, foreign body, fractured bone displacement, extraocular muscle entrapment, forced duction test, and so on. But TCR was triggered through a stimulus, a gentle force when removing a JP drain is first reported as described in the patient of our case report.

Chemical or inflammatory stimuli can also provoke a TCR, for instance, subdural empyema, exposure to hydrogen peroxide (H_2O_2), and parotid gland abscess.[47-49] Antecedent transient ischemic attacks within six weeks before an operation have been proposed as a triggering risk factor for subsequent intra-operative TCR.[50]Furthermore, certain drugs are also considered as TCR chemical stimulants, including potent narcotic agents (like sufentanil and alfentanil), β-blockers, as well as calcium channel blockers. Potent narcotics inhibit the sympathetic nervous system, whereas β-blockers decrease the sympathetic response of the heart and cause peripheral arterial vasodilatation, resulting in decreased HR and MABP.[42, 51] Overall, those drugs disturb the balance of autonomic outflow and TCR reflex circuitry, but evidence for the impact and mechanism of those drugs is still limited.[35]

Different depth of anesthesia is accountable for variable sympathetic outflow response,[52] while different types of anesthetics and analgesics differentially alter the neurotransmission to the neurons involved, they can either inhibit or facilitate TCR response.[53] For example, intravenous ketamine inhibits the synaptic transmission at both trigeminal afferent neurons and polysynaptic glutamatergic inputs to efferent cardiac vagal neurons (CVNs) in the nucleus ambiguus.[53] In contrast, fentanyl facilitates while isoflurane inhibits the reflex activation of CVNs.[53]

Electrical stimulation of trigeminal sensory fibers causes TCR through activating polysynaptic pathways in premotor parasympathetic CVNs. Even the electrical trigger at nerve fibers with small diameter, such as those within the anterior ethmoidal nerve of muskrats, can produce remarkable cardiovascular and respiratory responses.[54]According to the experiments conducted by Allen et. al., increased MABP and HR are detected when noxious electrical stimulation is given at mandibular incisor of anesthetized rats.[55, 56]

The central type of TCR during intracranial neurosurgical procedures is common and has been extensively discussed for decades. Previous reported neurosurgical procedures with apparent TCR episodes include cerebellopontine tumor resection, microvascular trigeminal decompression or Jannetta procedure, transphenoidal surgery, skull base procedures, supratentorial interventions, percutaneous procedures for trigeminal neuralgia management such as glycerol rhizolysis, balloon compression, radiofrequency ablation, and so forth.[36] Overall incidence of TCR is documented in relation to anatomical regions, 15% - 70% for middle cranial fossa, 11% - 18% for posterior cranial fossa, and 10% - 11% for cavernous sinus plexus.[5, 36]

Contrary to the central TCR, the peripheral TCR consists largely of OCR variant that generally occurs during ophthalmic surgery or manipulation of the orbital tissues. Most commonly observed procedures include corrective surgery for strabismus, intraorbital mass resection, ocular or orbital trauma, those surgeries with orbitozygomatic approach, empty orbital socket, etc. TCR incidence in orbital and periorbital region stands as high as 31% - 90%, but rarely cause mortality.[57]

On the other hand, MCR occurrence in maxillofacial procedures is relatively rare, with a reported incidence of 1% - 2% only.[58] Procedures that have induced the MCR events, include the LeFort-I osteotomy, bilateral sagittal split osteotomy, reduction for midface fractures, elevation of zygomatic fractures, parotidectomy, and temporomandibular joint surgery.[5]

So far, published reports of peripheral TCR episodes that are related to any manipulation in maxillofacial regions have been reviewed, and Table 2 lists published reports on TCR episodes.

Prevention and management

Many studies have advocated the essential management for TCR is to be aware of its potential danger and to minimize the stimulation of the nerve. Arasho et. al. have proposed a series of classification for the managing TCR,[28] which is further summarized in the Table 3.

In general, both local infiltrative anesthesia and block anesthesia have been proven to be effective in preventing of TCR, on the basis of surgical field. Peribulbar block with bupivacaine can remarkably reduce the OCR incidence as well as the reflex severity in retinal detachment and strabismus surgery.[59, 60] Intravenous (IV) drip of sodium nitroprusside (SNP) has been shown to be efficacious to prevent abrupt BP elevation.[41] Meanwhile, IV atropine sulfate that blocks the peripheral muscarinic receptors at heart, and retrobulbar xylocaine hydrochloride that blocks the conduction at ciliary ganglion, prophylactic use of both atropine and retrobulbar xylocaine have been shown to reduce the incidence of OCR. Besides, combination use of both methods may suppress the reflex completely.[61]

Similar to atropine, glycopyrrolate can also reduce the incidence of bradycardia.[62] But, the efficacies of intramuscular (IM) administration of those drugs are controversial. Especially the IM atropine, a cholinergic blockage can reduce bradycardia or hypotension.[63] On the other hand, glycopyrrolate 10 μg/kg given through IM route has shown to be effective in decreasing the occurrence rate.[64] For percutaneous compression of the trigeminal ganglion (PCTG) in treating trigieminal neuralgia, premedication with sodium nitroprusside (SNP) has been used to control fluctuations in blood pressure which benefits stable hemodynamics.[41] To prognosticate the occurrence of TCR, incorporation of serum surrogate biomarkers and intraoperative radiological markers can play a role.[65]

During the episodes, atropine is the treatment of choice for reflex bradycardia, and dopamine is suggested as a second line drug that should be used after atropine.[13] Still, refractory response to atropine has been reported in situations where the stimulation is intense.[66] Epinephrine that increases peripheral resistance and heart rate through alpha-1 adrenoceptor response, has been used to manage the reflex successfully,[66]verifying that the TCR involves in excessive vagal stimulation and reduced sympathetic tone. Thus, management that feasible for peripheral TCR is not necessarily applicable to central TCR. In cases with repeated and refractory symptomatic bradycardia, pacemaker insertion can be considered.[49] Although rare, severe and persistent TCRs requiring cardiac life support, have been reported in literature.[67] Fortunately, similar to our encountered circumstance, immediate cessation of manipulation is commonly sufficient in most cases to

restore stable HR and BP without the need of giving additional anticholinergic medication.[28]

Conclusion

Our patient was healthy without structural heart disease, his intra-operative blood pressure was considerably stable. But sudden hemodynamic fluctuation with bradycardia and consciousness change occurred immediately to a single removal of JP drain, however it was self-limited as most of the TCR, which aborted upon releasing the stimuli. Although strong and vigorous stimuli have shown to be one of the most important risk factors, however, the mild form of stimuli, although rare, can lead to sudden hemodynamic fluctuation.

In summary, comprehensive understanding of TCR is crucial to prompt efficacious treatment. Surgeons should be alert at risk identification, variability of its onset, as well as the different behavior of TCR based on the location and type of the stimuli applied. The most fundamental management for the TCR is to be aware of its potential risk before any associated procedure, minimize any stimulation of the nerve that could possibly lead to its occurrence, and to exploit preventive measures to avert it or constraint the intensity of the reflex.

Author contribution

Ying Chui Hong: Analysis and interpretation of data, drafting the article

Cheng-Yu Hsieh: Acquisition of data Chun-Jen Huang: Conception and design, revision of intellectual content Kuan-Chou Lin: Coordinator, Critical revision

Ethical approval: Approved by the TMU-Joint Institutional Review Board, IRB Reference number N202005117.

Funding information: No funding to report for this submission.

Acknowledgements:

No additional contribution other than the listed authors to be acknowledged.

Conflict of Interest

All of the authors have no conflict of interest to declare.

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Figure 1. Preoperative electrocardiogram record

Figure 2. Electrocardiogram recorded during the episode

Table 1. Evidence of TCR with the cause-effect relationship (Meuwly's description) [27]

Figure 3. Illustrated reflex arc of the TCR

Figure 4. The position of the JP drain catheter intra-operatively

Figure 5. The Classification of the TCR and Hemodynamic Changes

Table 2. Published reports on TCR episodes (January 1, 1970 - March 31, 2019)

* Other: hypertension, hypotension, gastric hypermobility, nausea or vomit, bronchospasm, hyponea, headache, change of consciousness

** PubMed search with the following keywords, while only English publication regarding the TCR within oral maxilla-facial region are included, other TCR reports related to neurosurgeries and intracranial approaches are excluded in this review.

*** (Case report) AND (trigeminocardiac reflex) OR (trigeminovagal reflex) OR (trigeminal depressor response) OR (oculocardiac reflex) OR (aschner reflex) OR (maxillomandibular reflex)

Table 3. Prevention and management for TCR

* CN, cranial nerve; CCB, calcium channel blocker; PCTG, percutaneous compression of trigeminal ganglion

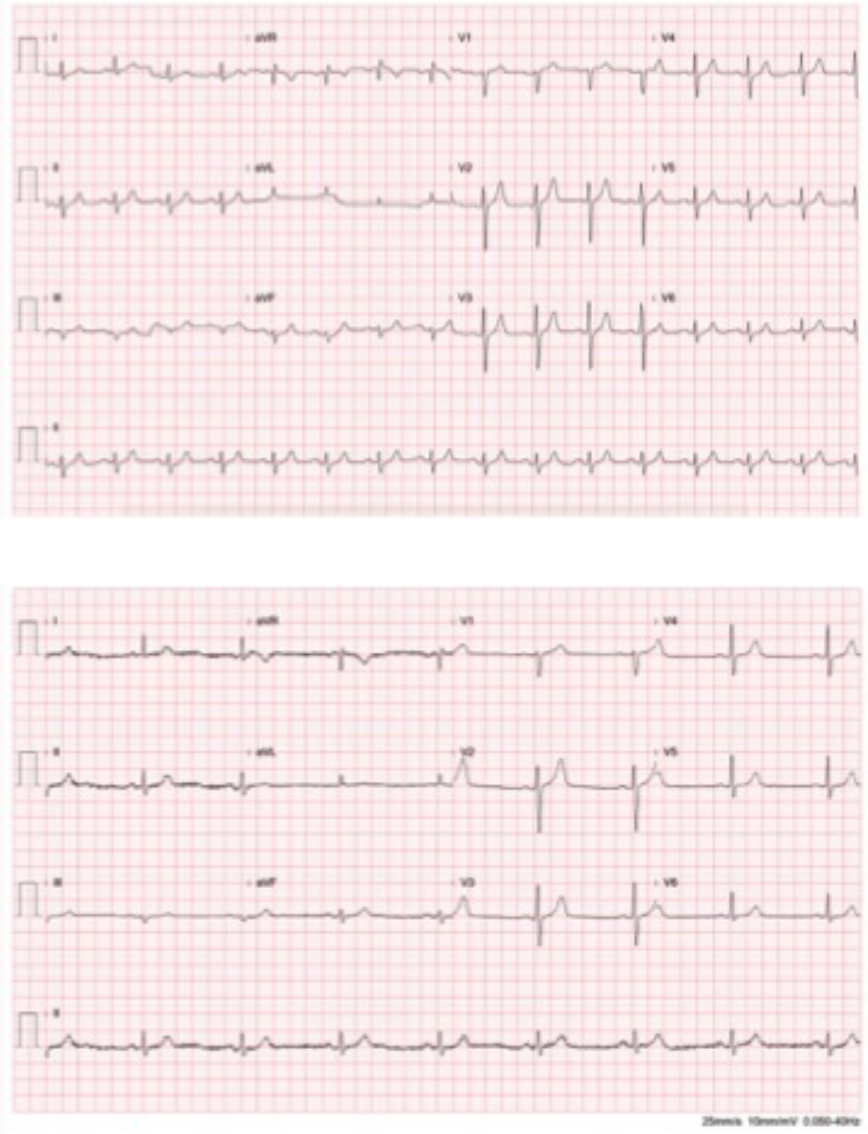

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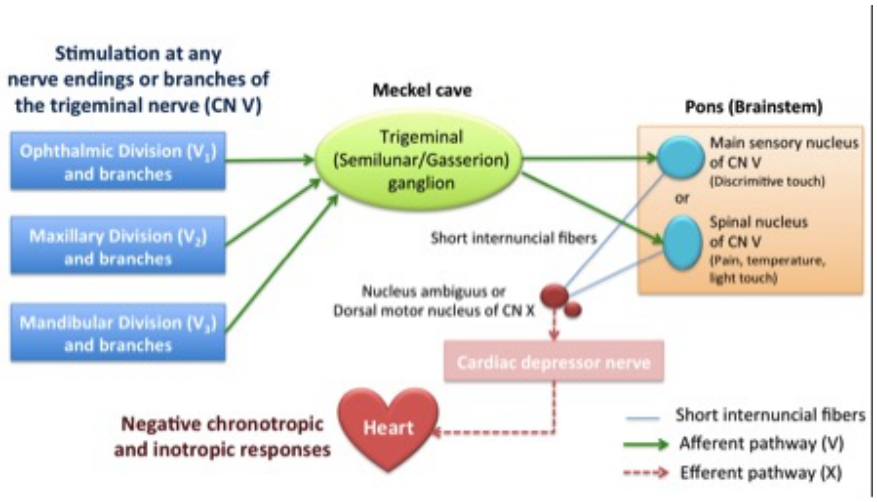
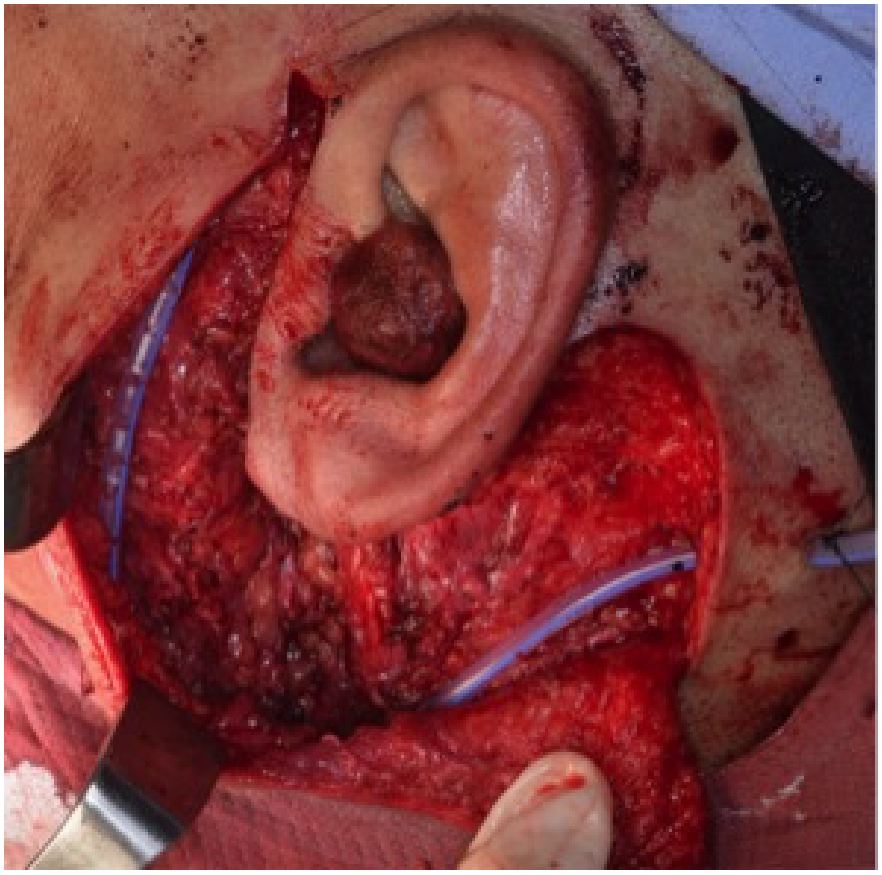
Table 1.pdf available at https://authorea.com/users/363119/articles/484009-trigeminocardiac-reflex-elicited-in-the-head-and-neck-region-a-case-report-triggered-by-the-removal-of-jackson-pratt-drain





	Central TCR	Brainstem Reflex	Gasserian Ganglion Reflex	Peripheral TCR		
				Oculocardiac Reflex	Maxillo-Mandibular-Cardiac Reflex	Diving Reflex
Stimuli	Intracranial stimulation, proximal to GG	Direct stimulation on brainstem	Direct stimulation on GG	Globe, ocular muscle, V_1 branches and innervated tissues	V_2, V_3 branches and innervated tissues	Anterior ethmoidal nerve in nasal mucosa
HR	↓	↓	↑ / ↓	↓	↓	↓
MABP	↓	↓	↑ / ↓	↔ / ↓	↔ / ↓	↑
Resp.	Bradypnea/ Apnea	Bradypnea/ Apnea	Bradypnea/ Apnea	Bradypnea/ Apnea	Bradypnea/ Apnea	Bradypnea/ Apnea

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