DOI: 10.5137/1019-5149.JTN.8008-13.1
Received: 25.02.2013 / Accepted: 20.04.2013

Review

Trigeminal Cardiac Reflex Caused by Onyx Embolization of Intracranial Dural Arteriovenous Fistula

Jian WANG[1,2], Huan-Cheng WU[3], Wei-Wei WANG[4], Hong-Sen ZHAO[5], Ri-Na DAO[5], Wei-Min LIU[5], Dong-Zhe ZHOU[5], Hui-Yu WANG[5], Chao DU[1]

[1]China-Japan Union Hospital of Jilin University, The Second Department of Neurosurgery, Changchun City, JiLin Province, China.
[2]The Affiliated Hospital of Inner Mongolia National University, Neurosurgery Department, Tongliao, Inner Mongolia, China
[3]Encephalopathy Center of the Affiliated Hospital of Medical College of the Chinese People's Armed Police Forces, Tianjin, China
[4]The Sixth People's Hospital of Shenyang, Department of Infectious Diseases, Shenyang City, Liaoning Province, China
[5]The Affiliated Hospital of Inner Mongolia National University, Tongliao, Inner Mongolia, China

ABSTRACT

Trigeminocardiac reflex (TCR) is a reflexive response of bradycardia, hypotension and gastric hypermotility which is observed upon mechanical stimulation in the distribution of the trigeminal nerve. Previous articles have described TCR during intracranial operations, ophthalmic surgery, microcompression of the trigeminal ganglion and radiofrequency lesioning of the trigeminal ganglion. TCR may occur during transarterial embolization of dural arteriovenous fistula (DAVF) with Onyx, leading to a significant decrease in heart rate under a standard anesthetic protocol. TCR may also occur due to chemical stimulus of dimethyl sulfoxide (DMSO) in transvenous Onyx embolization of dural cavernous sinus fistula. Slow rate of injection may give DMSO enough time to dissipate in the blood stream which is important for the prevention of toxicity. This report confirms that the reflex was blunted by the anticholinergic effects of atropine and there was no harm to patients if stopped immediately.

KEYWORDS: Trigeminal cardiac reflex, Onyx embolization, Intracranial dural arteriovenous fistula

INTRODUCTION

Trigeminocardiac reflex (TCR) has been described as a reflexive response of bradycardia, hypotension and gastric hypermotility following a mechanical stimulation in the distribution of the trigeminal nerve (3,5,6,14,37,38,39). TCR may be seen during intracranial operations, ophthalmic surgery, microcompression of the trigeminal ganglion and radiofrequency lesioning of the trigeminal ganglion (3,7,10-14,25,26,29,31-36,39) Induced TCR during corrections of craniofacial and maxillofacial deformities has been described (16,25,36) Until recently, TCR was described as a complication of Onyx embolization for dural arteriovenous fistula (DAVF) (2,19-22,24,27) To determine the nature and extent of TCR during Onyx embolization for DAVFs, a consecutive series of Onyx embolization under a standardized anesthetic protocol with special reference to incidence was reviewed retrospectively.

1. Arterial Supply of Dura Mater

Anterior meningeal branches of the anterior and posterior ethmoidal and internal carotid arteries and a branch of the middle meningeal artery supply the dura mater in the anterior cranial fossa (1). Middle and accessory meningeal branches of the maxillary artery, a branch of the ascending pharyngeal artery branches of the internal carotid and a recurrent branch of the lacrimal artery supply the dura mater of the middle cranial fossa. In the posterior fossa, the dura mater is supplied by the meningeal branches of the occipital, the posterior meningeal branches of the vertebral artery, and sometimes small branches of the ascending pharyngeal artery (1, 33).

Corresponding author: Chao DU
E-mail: duchao0987@yahoo.com

2. Nerve Innervation of Dura Mater

The dura mater of the anterior and middle cranial fossa, as well as superior aspect of the tentorium, receives sensory innervation from the intracranial branches of all divisions of the trigeminal nerve. Sensory innervation of the dura mater of posterior cranial fossa is by the branches of cervical spinal nerves C2 and C3, and possibly a small component from the vagus nerve. There is increased sensitivity to pain in the dura mater along the superior sagittal sinus and the tentorium (1,3,40-42).

3. Intracranial Dural Arteriovenous Fistula

Dural arteriovenous fistulae are abnormal connections between dural arteries and venous sinuses, accounting for 10–15% of all intracranial arteriovenous shunts. It is believed that these connections are secondary to trauma or dural sinus thrombosis (19). These connections are called DAVF because of the dural sinus in which the arteriovenous shunts exist (19).

The clinical symptoms of DAVFs can be secondary to intracerebral hemorrhage (ICH). The symptoms are ocular symptoms, bruits, hemihypesthesia, hemifacial spasm, trigeminal neuralgia and headaches due to increased intracranial pressure (18,19). The venous drainage pattern of DAVFs determines their risk of hemorrhage, and this characteristic underlies the classification system of Cognard et al. (Table I) (8).

4. Natural History of Intracranial Dural Arteriovenous Fistula

Aggressive/non-aggressive behavior was 1/8.8 for fistulae located into the transverse or sigmoid sinus (4,9,20). Aggressive behavior was found in 40%, 30%, and 70% of Merland type IIa, IIb, and IIa+b fistulae, respectively, and in 80% and 95% of types III and IV, respectively (20). Bleeding was seen in 20% of type II lesions, and in 40% and 66% of types III and IV, respectively. The Toronto group demonstrated an annual risk of 6.9% for non-hemorrhagic neurological deficit, 8.1% for hemorrhage, and an annual mortality rate of 10.4% among 118 patients of DAVFs with leptomeningeal reflux (43). These reports support the need for active and curative treatment of DAVFs when associated with leptomeningeal and/or cortical venous reflux. Conservative management is recommended for DAVFs without venous drainage. A high hemorrhagic risk of 10%–40% and significant morbidity and mortality are seen in dural transverse sinus arteriovenous fistula with cortical venous drainage (15). In the presence of associated spinal perimedullary drainage, these fistulae may present with brainstem ischemia and myelopathy (20).

5. Shift to Onyx Embolization

Dural arteriovenous fistulas can be treated using transarterial or transvenous embolization. Onyx is a non-adhesive liquid embolic agent and does not polymerize. This property allows the surgeon far greater latitude in varying the rate of injection and the amount of the agent delivered in a single injection. The ethylene vinyl alcohol copolymer precipitates, whereas dimethyl sulfoxide can diffuse under aqueous conditions and occlude mechanically the feeders (19). If the microcatheter is placed sufficiently distally, longer reflux of Onyx around the tip of the microcatheter can be achieved more safely in the external carotid artery territory as compared with the pial arteries. This long reflux may create sufficient proximal flow to enable better distal penetration (19). Our initial experience with the use of Onyx for embolization of intracranial DAVFs is encouraging, with complete obliteration with transarterial Onyx embolization in 62.5% (21) and transvenous Onyx embolization in 100% (22).

6. Anesthetic Technique

All patients were placed under a standardized anesthesia protocol. Patients fasted for at least six hours prior to procedure. Electronically recorded routine monitoring (Spacelabs, Redmond, WA, USA) during the endovascular procedure included electrocardiogram (ECG), heart rate (HR), arterial blood pressure, and pulse oximetry (oxygen saturations >96%). Distinct intraprocedural episodes of more than 20% decrease of HR compared with baseline values before the stimulus, and the number of such episodes requiring interventional therapy were evaluated from a blinded anesthesia record retrospectively. Anesthesia was induced with propofol (2mg/Kg), remifentanyl (3 μg/Kg) and atracurium (0.5 mg/Kg). After the trachea was intubated, the lungs were mechanically ventilated with a mixture of air and oxygen (FIO2 =0.5) (34). Anesthesia was maintained with remifentanyl (0.1 μg/Kg/min) and propofol (6 mg/Kg/h); additional boluses of remifentanyl and atracurium were administered when necessary.

7. Trigeminal Cardiac Reflex in Transarterial Onyx Embolization

TCR was seen upon Onyx injection via the middle meningeal artery during embolization of DAVF. The TCR rate is 7.7% (95% CI, 2 to 21%) in patients treated with intraarterial Onyx embolization (23). The phenomenon of bradycardia during Onyx injection resolved upon cessation of injection. This response of bradycardia was reproducible.

Table I: Cognard Classification of DAVF (1995)

I. Venous drainage into dural venous sinus with antegrade flow
IIa. Venous drainage into dural venous sinus with retrograde flow
IIb. Venous drainage into dural venous sinus with antegrade flow and CVR
IIa+b. Venous drainage into dural venous sinus with retrograde flow and CVR
III. Venous drainage directly into subarachnoid veins (CVR only)
IV. Type III with venous ectasias of the draining subarachnoid veins

After intravenous administration of atropine, the response was no longer reproducible, and the procedure could be completed (27). The reflex bradycardia seen during Onyx injection is not likely attributable to other factors. Studies of anesthesia monitoring in patients treated with Onyx embolization for intracranial aneurysms showed no changes in HR or blood pressure following dimethyl sulfoxide (DMSO) and Onyx injections, nor were any arrhythmias observed (27,28). We consider that this response was a TCR and the reflex was reproducible during pushing Onyx via the pedicle of the middle meningeal artery, so the reflex probably began from the dura mater. Penfield and McNaughton (30) showed the nervous innervation of the dura mater and a rational pathway from the dura to the vagal motor nucleus (3,27). We think that direct distraction by the dilated middle meningeal artery due to formation of Onyx plug produces an injection pressure, which induces neuronal signals via the Gassarian ganglion to the sensory nucleus of the trigeminal nerve, forming the afferent pathway of the reflex arc. When dural stimulation causes TCR, the treatment of hemodynamic instability is to stop the procedure and administer an anticholinergic drug. Atropine extinguished the TCR in our patient. Anticholinergic drugs are not given prophylactically due to risk of refractory arrhythmias (3,27).

8. Trigeminal Cardiac Reflex in Transvenous Onyx Embolization

Cavernous DAVF treatment is primarily transvenous coiling (17). Our experience encouraged us to use Onyx in the treatment of cavernous DAVF. The slow injection of the agent might have been the key factor that enabled casting

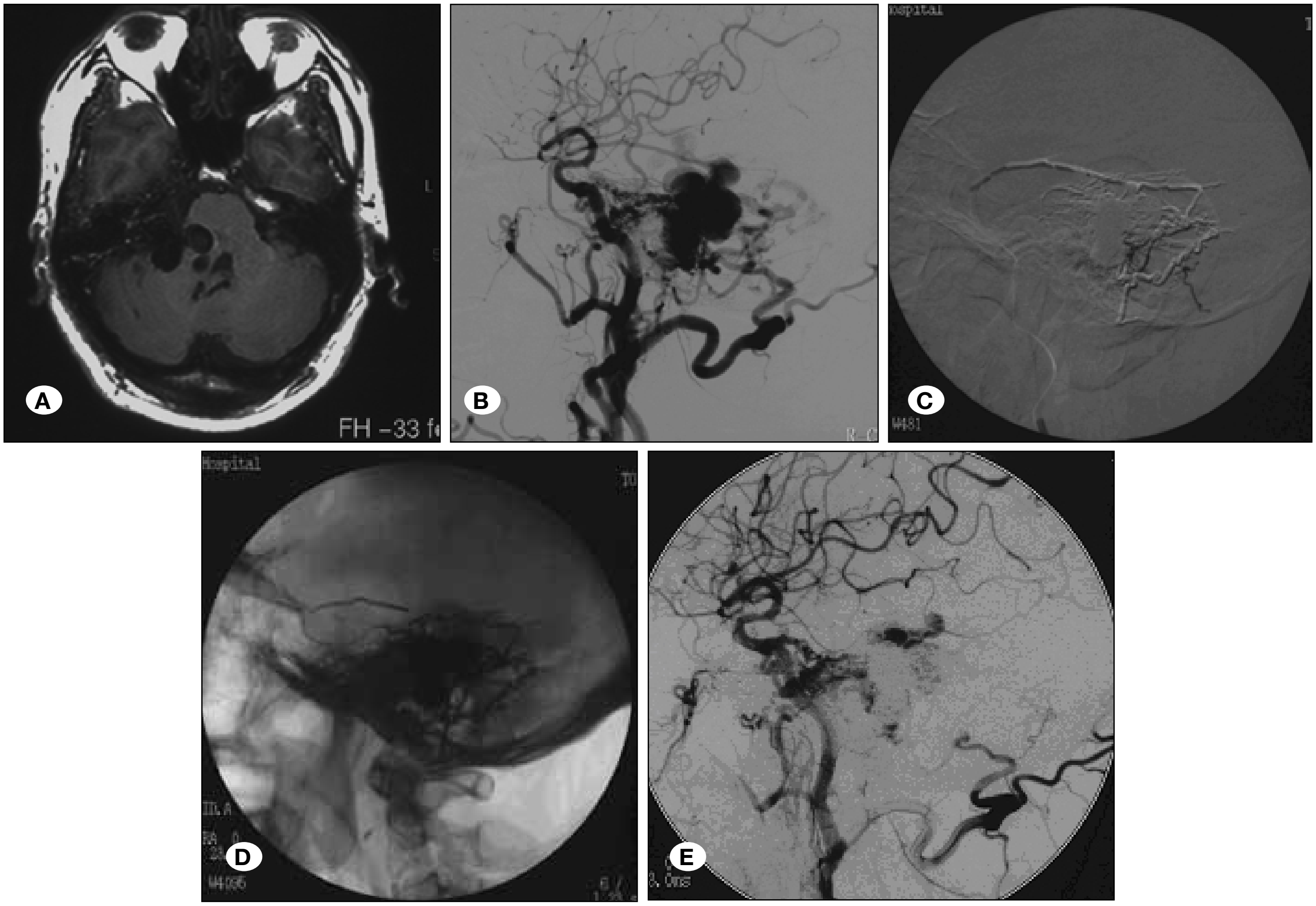

Figure 1: A 47-year-old man presented with right trigeminal neuralgia. **A)** Axial T1- weighted non-enhanced MRI showed flow-void signals at the cerebellopontine angle. **B)** Subtracted angiography of the right common carotid artery showed a Cognard type IV petrosal DAVF, which was supplied by the middle meningeal artery and dural branches arising form the right ascending pharyngeal artery, occipital artery and internal carotid artery and drained via the dilated petrosal vein. The middle meningeal artery was selectively catheterized with a microcatheter (Marathon, MTI-EV3, Irvine, CA, USA) through a guiding catheter. Embolization was undertaken with Onyx-18 (MTI-EV3, Irvine, CA, USA) using “push- reflex-push” technique. **C)** The fluoroscopic image was obtained while his heart rate decreased down to 40 bpm. We had to cease Onyx injection and atropine was administered transvenously. **D)** Unsubtrated image showed the Onyx cast after embolization. **E)** Postembolization angiogram showed that the fistula was nearly complete occluded. His trigeminal neuralgia disappeared on the next day after treatment.

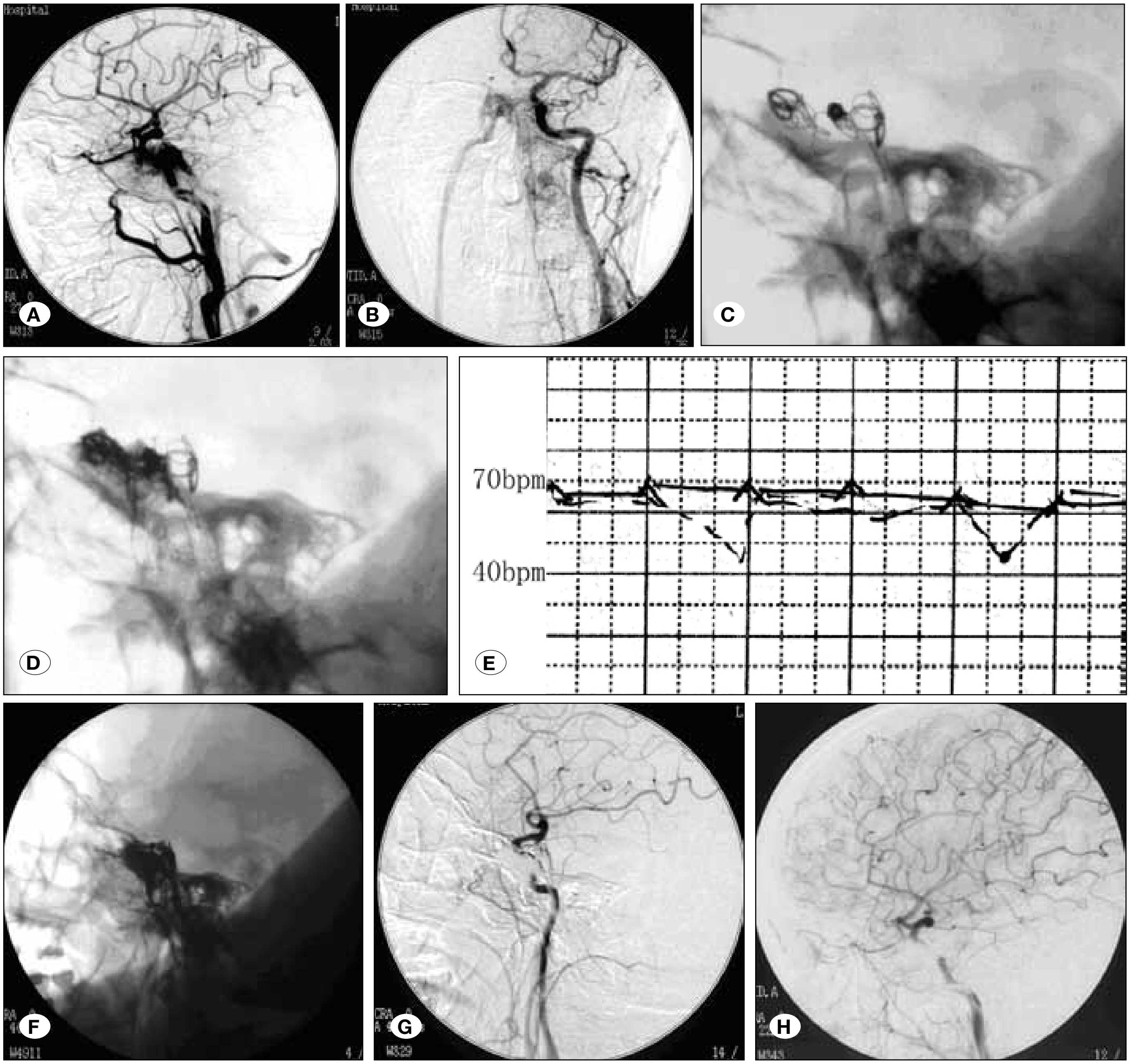

Figure 2: A 54-year-old man presented with right CN III palsy. **A)** Subtracted angiography of the right common carotid artery, lateral view, showed a dural cavernous fistula, which was supplied by the dural branches arising form the external carotid and internal carotid arteries and drained via the inferior petrosal sinus. **B)** Subtracted angiography of the left common carotid artery, frontal view, showed the dural suppliers arising form left carotid artery. Two 6- French sheaths were placed in the left femoral artery and right femoral vein. A 5-French catheter was placed in the right carotid artery, allowed acquisition of roadmaps, and angiographic monitoring of the procedure. A second 5-French guiding catheter was positioned in the right jugular vein. A microcatheter (Echelon10, MTI-EV3, Irvine, CA, USA) was navigated coaxially via the right inferior petrosal sinus approach. The microguidewire (Silverspeed10, MTI-EV3, Irvine, CA, USA) was then carefully introduced and advanced to the cavernous portion, followed by the microcatheter (20). Then, under biplane road mapping, all embolizations were performed with a combination of detachable coils and Onyx-18 using realtime digital subtraction fluoroscopic mapping. Patency of the right internal carotid artery was checked frequently during the intermittent injection of the embolic material. **C)** Unsubtrated image showed the coils prior to Onyx injection. **D)** Unsubtrated image showed the Onyx cast after coil delivery. **E)** The angiogram was obtained to record his heart rate decreased down to 40 bpm two times during treatment. After intravenous administration of atropine, the response was no longer reproducible, and the procedure could be completed. **F)** After embolization, the unsubtrated image, lateral view, demonstrated the Onyx cast. **G)** Postembolization angiogram of the right carotid artery reveals complete embolization of the fistula. **H)** 7-month follow-up angiogram confirmed the complete obliteration and his CN III palsy recovery completely.

of the sinus, with filling of its interstices and blocking of the minute fistulous communications (17,22). The TCR seen in our patients developed when a minimal amount (possibly 0.25 –0.3 mL) of DMSO might have entered the cavernous sinuses (CS). This amount of DMSO within the CS may cause sufficient mechanical stimulation on the adjacent trigeminal nerve to elicit the TCR. DMSO has the ability to diffuse rapidly through tissues. It may provoke the TCR via chemical irritation of the trigeminal nerve (particularly ophthalmic and maxillary divisions in the lateral wall of the CS) because of its neurotoxicity (22). Rapid intravascular administrations of DMSO have also been shown to be associated with histotoxicity. So, DMSO should be injected slowly to allow it to dissipate gradually in the CS, and thereby reduce its potential toxic or irritant effect on the trigeminal nerve (22).

We think that neurotoxicity of DMSO on the ophthalmic nerve within the CS or on the trigeminal nerve innervation of the dura mater causes and sends neuronal signals via the Gassarian ganglion to the sensory nucleus of the trigeminal nerve. This forms the afferent pathway of the reflex arc (24).

This pathway continues along the short internuncial nerve fibers in the reticular formation to connect with the efferent pathway in the motor nucleus of the vagus nerve and causes bradycardia (27). This phenomenon of bradycardia was not observed in transvenous GDC and NBCA embolization of cavernous DAVF (44,45). TCR was observed in 33.3% (95% CI, 4 to 78%) of the patients treated with intravenous Onyx embolization (23,27).

■ CONCLUSION

TCR may occur during transarterial Onyx embolization of DAVF, leading to a significant decrease in the heart rate under a standard anesthetic protocol. TCR may also occur due to chemical stimulus of DMSO in transvenous Onyx embolization of dural cavernous sinus fistula. A slow rate of injection may give DMSO enough time to dissipate in the blood stream. This slow injection is important for the prevention of toxicity. This study confirms that the reflex was blunted by the anticholinergic effects of atropine and there was no harm to the patients if stopped immediately.

■ REFERENCES

1. Adeeb N, Mortazavi MM, Tubbs RS, Cohen-Gadol AA: The cranial dura mater: A review of its history, embryology, and anatomy. Childs Nerv Syst 28(6):827-837, 2012
2. Amiridze N, Zoarski G, Darwish R, Obuchowski A, Soloveychic N: Embolization of a cavernous sinus dural arteriovenous fistula with Onfyx via direct puncture of the cavernous sinus through the superior orbital fissure: Asystole resulting from the trigeminocardiac reflex. A case report. Interv Neuroradiol 15:179-184, 2009
3. Bauer DF, Youkilis A, Schenck C, Turner CR, Thompson BG: The falcine trigeminocardiac reflex: Case report and review of the literature. Surgical Neurology 63: 143– 148,2005
4. Bernstein R, Dowd CF, Gress DR: Rapidly reversible dementia. Lancet 361:392, 2003
5. Blanc VF: Trigeminocardiac reflexes. Can J Anaesth 38: 696-699, 1991
6. Brown JA, Preul MC, Nimr S: Trigeminocardiac reflexes. Can J Anaesth 39: 303-305, 1992
7. Cha ST, Eby JB, Katzen JT, Shahinian HK: Trigeminocardiac reflex: A unique case of recurrent asystole during bilateral trigeminal sensory root rhizotomy. J Craniomaxillofac Surg 30:108-111, 2002.
8. Cognard C, Gobin YP, Pierot L, Bailly AL, Houdart E, Casasco A, Chiras J, Merland JJ: Cerebral dural arteriovenous fistulas: Clinical and angiographic correlation with a revised classification of venous drainage. Radiology 194:671-680, 1995
9. Djindjian R, Merland JJ: Superselective arteriography of the external carotid artery. Berlin: Springer, 1978
10. Fowler SJ, Featherston M: Recurrent atrial tachyarrhythmia triggered by percutaneous balloon rhizotomy of the trigeminal nerve. Anaesth Intensive Care 32: 410-412, 2004
11. Gharabaghi A, Acioly MA, Koerbel A, Tatagiba M: Prognostic factors for hearing loss following the trigeminocardiac reflex. Acta Neurochir (Wien) 149: 737, 2007
12. Gharabaghi A, Acioly de Sousa MA, Tatagiba M: Detection and prevention of the trigeminocardiac reflex during cerebellopontine angle surgery. Acta Neurochir (Wien) 148: 1223, 2006
13. Gharabaghi A, Koerbel A, Samii A, Kaminsky J, von Goesseln H, Tatagiba M, Samii M: The impact of hypotension due to the trigeminocardiac reflex on auditory function in vestibular schwannoma surgery. J Neurosurg 104: 369-375, 2006
14. Koerbel A, Gharabaghi A, Samii A, Gerganov V, von Gösseln H, Tatagiba M, Samii M: Trigeminocardiac reflex during skull base surgery: Mechanism and management. Acta Neurochir (Wien) 147: 727-732, 2005
15. Lalwani AK, Kowd CF, Halbach VV: Grading venous restrictive disease in patients with dural arteriovenous fistulas of the transverse/sigmoid sinus. J Neurosurg 79:11-15, 1993
16. Lang S, Lanigan DT, van der Wal M: Trigeminocardiac reflexes: Maxillary and mandibular variants of the oculocardiac reflex. Can J Anaesth 38: 757-760, 1991
17. Li L, Cui JG, Liang ZH, Xu SB, Li J, Tian HQ, Fan YH: Transvenous treatment of complex cavernous dural arteriovenous fistulae with Onyx and coils. Neurol India 59(1):92-96, 2011
18. Li T, Lv X, Wu Z: Endovascular treatment of hemifacial spasm associated with a petrosal DAVF using transarterial Onyx embolization: Case report. Interv Neuroradiol 18:69-73, 2012
19. Lv X, Jiang C, Li Y, Wu Z: Results and complications of transarterial embolization of intracranial dural arteriovenous fistulas using Onyx-18. J Neurosurg 109:1083-1090, 2008
20. Lv X, Jiang C, Li Y, Liu L, Liu J, Wu Z: Transverse-sigmoid sinus dural arteriovenous fistulae. World Neurosurg 74(2-3):297-305, 2010
21. Lv X, Jiang C, Zhang J, Li Y, Wu Z: Complications related to percutaneous transarterial embolization of intracranial dural arteriovenous fistulas in 40 patients. Am J Neuroradiol 30: 462 – 468, 2009
22. Lv X, Jiang C, Li Y, Wu Z: Percutaneous transvenous packing of cavernous sinus with Onyx for cavernous dural arteriovenous fistula. Eur J Radiol 71:356-362, 2009
23. Lv X, Li Y, Jiang C, Wu Z: The incidence of trigeminocardiac reflex in endovascular treatment of dural arteriovenous fistula with Onyx. Interv Neuroradiol 16:59-63, 2010

24. Lv X, Li Y, Lv M, Liu A, Zhang J, Wu Z: Trigeminocardiac reflex in embolization of intracranial dural arteriovenous fistula. Am J Neuroradiol 28: 1769-1770, 2007

25. Lynch MJ, Parker H: Forensic aspects of ocular injury. Am J Forensic Med Pathol 21: 124- 126, 2000

26. Madhusudan Reddy KR, Chandramouli BA, Umamaheswara GS: Cardiac asystole during radiofrequency lesioning of the trigeminal ganglion. J Neurosurg Anesthesiol 18: 163-164, 2006

27. Ong CK, Ong MT, Le K, Power MA, Wang LL, Lam DV, Parkinson RJ, Wenderoth JD: The trigeminocardiac reflex in Onyx embolisation of intracranial dural arteriovenous fistula. J Clin Neurosci 17:1267–1270, 2010

28. Pamuk AG, Saatci I, Cekirge HS, Aypar U: A contribution to the controversy over dimethyl sulfoxide toxicity: Anesthesia monitoring results in patients treated with Onyx embolization for intracranial aneurysms. Neuroradiology 47:380–386, 2005

29. Panneton WM, Yavari P: A medullary dorsal horn relay for the cardiorespiratory response evoked by stimulation of the nasal mucosa in the muskrat Ondatra zibethicus: Evidence for excitatory amino acid transmission. Brain Res 691: 37-45, 1995

30. Penfield W, McNaughton F: Dural headache and innervation of the dura matter. Arch Neurol Psychiatr 44:43–75, 1940

31. Prabhakar H, Anand N, Chouhan RS, Bithal PK: Sudden asystole during surgery in the cerebellopontine angle. Acta Neurochir (Wien) 148: 699-700, 2006

32. Roberts RS, Best JA, Shapiro RD: Trigeminocardiac reflex during temporomandibular joint arthroscopy: Report of a case. J Oral Maxillofac Surg 57: 854-856, 1999

33. Schaller B: Trigemino-cardiac reflex during microvascular trigeminal decompression in cases of trigeminal neuralgia. J Neurosurg Anesthesiol 17: 45-48, 2005

34. Schaller B: Trigemino-cardiac reflex during transsphenoidal surgery for pituitary adenomas. Clin Neurol Neurosurg 107: 468-474, 2005

35. Schaller B, Probst R, Strebel S, Gratzl O: Trigeminocardiac reflex during surgery in the cerebellopontine angle. J Neurosurg 90: 215-220, 1999

36. Schaller BJ, Buchfelder M: Delayed trigeminocardiac reflex induced by an intraorbital foreign body. Case report. Ophthalmologica 220: 348, 2006

37. Schaller B: Trigeminocardiac reflex. A clinical phenomenon or a new physiological entity? J Neurol 251: 658-665, 2004

38. Schaller BJ: Trigeminocardiac reflex. Neurosurgery 107:243, 2007

39. Schaller BJ, Filis A, Buchfelder M: Detection and prevention of the trigeminocardiac reflex during skull base surgery. Acta Neurochir (Wien) 149: 331, 2007

40. Schuenke M, Schulte E, Schumacher U: Head and Neuroanatomy (THIEME Atlas of Anatomy). Stuttgart: Thieme, 2006:190

41. Simons T, Ruskell LG: Distribution and termination of trigeminal nerves to the cerebral arteries in monkeys. J Anat 159:57-71, 1988

42. Taurig HH: The trigeminal system. In: Conn PM (ed). Neuroscience in Medicine. Totowa, NJ: Humana Press, 2008:287-299

43. van Dijik JMC, TerBrugge K, Willingsky RA, Wallance MC: Clinical course of cranial dural arteriovenous fistulas with long-term persistent cortical venous reflex. Stroke 33:1233- 1236, 2002

44. Wakhloo AK, Perlow A, Linfante I, Sandhu JS, Cameron J, Troffkin N, Schenck A, Schatz NJ, Tse DT, Lam BL: Transvenous n-butyl-cyanoacrylate infusion for complex dural carotid cavernous fistulas: Technical considerations and clinical outcome. AJNR Am J Neuroradiol 26:1888-1897, 2005

45. Yoshida K, Melake M, Oishi H, Yamamoto M, Arai H: Transvenous embolization of dural carotid cavernous fistulas: Series of 44 consecutive patient. AJNR Am J Neuroradiol 31:651-655, 2010