The Incidence of Trigeminocardiac Reflex in Endovascular Treatment of Dural Arteriovenous Fistula with Onyx

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Summary

This paper reports the incidence of trigeminocardiac reflex (TCR) in endovascular treatment of dural arteriovenous fistulas (DAVFs) with Onyx.

The consecutive case histories of 45 patients with DAVFs, treated with Onyx transarterially and transvenously, from February 2005 to February 2008 at Beijing Tiantan Hospital, China, were retrospectively reviewed. The time period was limited as the anesthetic and intravascular procedure was performed under the same standardized anesthetic protocol and by the same team. The TCR rate was subsequently calculated.

Of the 45 patients, five showed evidence of TCR during transarterial Onyx injection and transvenous DMSO injection. Their HR fell 50% during intravascular procedures compared with levels immediately before the stimulus. However, blood pressure values were stable in all cases. The TCR rate for all patients was 11.1% (95% CI, 4 to 24%), 7.7% (95% CI, 2 to 21%) in patients treated intraarterially and 33.3% (4 to 78%) in patients treated intravenously. Once HR has fallen, intravenous atropine is indicated to block the depressor response and prevention further TCR episodes.

TCR may occur due to chemical stimulus of DMSO and Onyx cast formation under a standardized anesthetic protocol and should be blunted by atropine.

Introduction

Trigeminocardiac reflex (TCR) has been described in the literature as a reflexive response of bradycardia, hypotension and gastric hypermotility seen upon mechanical stimulation in the distribution of the trigeminal nerve [1-6]. Previous articles have described TCR during intracranial operations, ophthalmic surgery, microcompression of the trigemimal ganglion and radiofrequency lesioning of the trigeminal ganglion [3,6,7-13,15-24]. TCR can be elicited by stimulating the afferent pathway not only from ciliary nerves but also from sensory branches of maxillary and mandibular divisions of the trigeminal nerve [15]. Induced TCR during corrections of craniofacial and maxillofacial deformities has been described [14,15,22,24]. But until recently, TCR was described as a complication of Onyx embolization for DAVFs [25]. 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. This is the first series of TCR caused by endovascular technique in intracranial DAVFs treatment.

Patients and Methods

Patient Population

From February 2005 to February 2007, we treated 45 patients with the intracranial DAVFs

at Beijing Tiantan Hospital. Transarterial embolization with Onyx-18 was performed in 39 patients and transvenous embolization with a combination with coils and Onyx in six patients. Patients comprised 11 women and 34 men, ranging in age from 23 to 69 years (31.8 ± 19.4years). Fifteen patients (33.3%) presented with intracranial hemorrhage, four (8.9%) had headaches without imaging evidence of bleeding, 15 (33.3%) had ocular symptoms, including chemosis, protosis, ophthalmoplegia and hemianopsia, 12 (26.7%) had tinnitus and intracranial bruits, one (2.2%) had hemihypoesthesia and one (2.2%) had trigeminal neuralgia. Venous drainage patterns were classified according to the Cognard Type system. One patient had Type V fistula, 18 patients had Type IV fistulae, three had Type III fistulae, 18 had Type IIa fistulae and three had Type I fistulae. The clinical follow-up periods after endovascular treatment range from one to 14 months (6.6 ± 3.8 months).

TCR was defined as a drop in mean arterial blood pressure (MABP) and heart rate (HR) of more than 20% compared with the baseline values before the stimulus and coinciding with the manipulation of the trigeminal nerve. Cessation of compression or traction of the trigeminal nerve had to result in a spontaneous increase in HR and MABP to normal levels. The phenomenon had to recur when compression or traction was repeated. Only the data of the first spontaneous occurrence of the reflex were used in the current study.

Anesthetic Technique

All patients were placed under a standardized anesthesia protocol. Patients fasted for at least six hours prior to procedure. Electronic recorded routine monitoring (Spacelabs, Redmond, WA, USA) during endovascular procedure included electrocardiogram (ECG), 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 (2 mg/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). 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.

Endovascular Technique

Transarterial Embolization

Feeding arteries were selectively catheterized with a microcatheter (Marathon/Echlon10, MTI-EV3, Irvine, CA, USA) through a guiding catheter, which was positioned in the external carotid artery or vertebral artery. Embolization was undertaken with a nonadhesive embolic agent (Onyx-18, MTI-EV3, Irvine, CA, USA).

Transvenous Embolization

We first placed two 6-French sheaths in the left femoral artery and right femoral vein. A 5-French catheter, placed in the carotid artery, allowed acquisition of roadmaps, and angiographic monitoring of the procedure. A second 5-French guiding catheter was positioned in the jugular vein. A microcatheter (Echelon10/Marathon, MTI-EV3, Irvine, CA, USA) was navigated coaxially via the venous approach. The microguidewire (Silverspeed10/Mirage, MTI-EV3, Irvine, CA, USA) was then carefully introduced and advanced to the cavernous portion, followed by the microcatheter. Then, under biplane roadmapping, all embolizations were performed with a combination of detachable coils and Onyx (Onyx18 or 34) using real-time digital subtraction fluoroscopic mapping. Patency of the right internal carotid artery was checked frequently during the intermittent injection of the embolic material.

Results

In our series, five patients [11.1% (95%CI, 4 to 24%)] showed evidence of TCR during transarterial Onyx injection or transvenous DMSO injection. Characteristics of the five patients (one woman and four men; age range, 42-57 yrs, 50 ± 5.3 yrs) with TCR are summarized in Table1. There was no history of arrhythmias. Symptoms included IIIrd cranial nerve palsy (n = 2), chemosis (n = 1), pulsatile tinnitus (n = 1) intracranial hemorrhage (n = 1) and trigeminal neuralgia (n = 1). According to the Cognard classification, the DAVFs were Type IIa (n = 3), Type IV (n = 1) and Type V (n = 1). The clinical

Table1 **Clinical courses and outcomes of 5 patients with TCRs.**

Pat. No.	Age/ Sex	Location	Presentation	Type*	Suppliers Type	Venous drainage	Treatment strategy	Complications	Follow-up	Clinical outcome
1.	42/M	Tentorium (R)	Intracerebellar hemorrhage	Cognard IV	ECA (R), ICA (R) SCA (R)	Cerebellar veins, PV, varix	Transartrials: right MMA; Onyx-18; success; incomplete	TCR, hemifacial hypoesthesia, hemifacial palsy	8 month	No symptoms, hemifacial hypoesthesia, resolved within 2 months; hemifacial palsy, resolved within 3 months
2.	50/F	InfPS(R)	Headaches, tinnitus, chemosis	Cognard IIa	VA (R), ECA (R) ICA (R)	InfPS, SOV	Transarterial: right MMA; Onyx-18; success; incomplete	TCR, hemifacial hypoesthesia, hemifacial palsy	8 month	Mild hemifacial palsy; hemifacial hypoesthesia resolved within 2 months
3.	47/M	Tentorium (R)	Trigeminal, neuralgia	Cognard V	ECA (R), ICA (R)	BVR, varix CV,SV	Transartrials: right MMA; Onyx-18; success; incomplete	TCR	1 month	No symptoms
4.	54/M	CS (L)	CNIII plasy (L)	Cognard IIa	ICA (B)	InfPS	Transvenous: left InfPS; Coils and Onyx; success; complete	TCR	13 month	Left CNIII palsy resolved within 4 month
5.	57/M	CS (R)	CNIII plasy (R)	Cognard IIa	ICA (B), ECA (B)	InfPS	Transvenous: right InfPS; Coils and Onyx; success; complete	TCR	5 month	Right CNIII resolved within 2 month

** Cognard classification.*
R, right; L, left; B, bilateral; F, female; M, male;CS, cavernous sinus; SOV, superior ophthalmic vein; InfPS, inferior petrosal sinus; ICA:internal carotid artery; ECA:external carotid artery; VA, vertebral artery; CNIII, the third cranial nerve; PV, petrosal vein; CV, cortical vein; SP, spinal vein; BVR, basal vein of Rosenthal; MMA, middle meningeal artery; SCA, superior cerebellar artery; TCR, trigemino-cardiac reflex.

follow-up periods range from one to 14 months (7 ± 3.9 months).

During Onyx and DMSO injections, patients' HR decreased significantly, as defined in the inclusion criteria, but in our series the mean arterial blood pressure decrease was not observed. When TCR occurred, HR fell to 35.4 beats/min (SD, 2.2 beats/min; range, 32-39 beats/min) during the procedure, returning to a mean of 72 beats/min (SD, 5.5 beats/min; range, 65-80 beats/min) after the end of the procedure. In one case, as DMSO was injected into the cavernous sinus, severe bradycardia occurred and heart rate dropped to 32 bpm. Cessation of DMSO injection and intravenous administration of atropine 0.5 mg restored the heart rate to 76 bpm over 30 seconds. His blood pressure at this time was 120/75 mmHg. Then when DMSO was injected again another episode of bradycardia occurred. Heart rate dropped to 45 bpm, we stopped injection of DMSO immediately and heart rate returned to normal. This was followed by injection of Onyx-34, and the reflexive bradycardia did not recur. The follow-up of this patient was uneventful. HR during a further procedure after the occurrence of TCR was not significantly differently from before.

Intravenous administration of atropine (0.6 mg; SD, 0.2 mg; range, 0.5-1.0 mg) led to a cessation of the reflex during the remainder of the surgical procedure in all five cases of TCR. Routine monitoring of ECG during postproedure 24 hours showed no sinus arrhythmia. Subsequent follow-up of the patients was uneventful. Further complications, which could be attributed to the occurrence of TCR, were not detected.

Discussion

TCR has been described as a physiological reflex [5]. Different experimental studies have analyzed the autonomic response elicited by the electrical, mechanical, or chemical stimulation of the trigeminal nerve system [1,2,4,5,17]. Clinically, the trigeminocardiac reflex has been reported to occur in ocular surgery, craniofacial surgery[11,13,16,22], tumor resection in the cerebellopontine angle [12,18,23,24] and falx cerebri [1,5], transsphenoidal surgery for pituitary adenomas [21] and microvascular trigeminal decompression for trigeminal neuralgia [20]. Current theories on the mechanism of trigeminocardiac reflex display a rational pathway of the nerve from the Gassarian ganglion to the vagal motor nucleus [5,17,26]. Recently, the occurrence of TCR during surgery in the cerebellopontine angle has been described [12,23], pointing out one possible reason why Onyx emblization of DAVFs near this region can also induce TCR. Propofol sedation is commonly employed in general anesthesia, but it does not prevent cardiovascular disturbance caused by stimulation to the trigeminal nerve. We think that neurotoxicity of DMSO on the cranial nerves within the cavernous sinus or direct compression of the trigeminal nervous innervation of the dural mater by the formation of an Onyx plug produces and sends neuronal signals via the Gassarian ganglion to the sensory nucleus of the trigeminal nerve, forming the afferent pathway of the reflex arc. This afferent 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.

Animal models have shown that abrupt and sustained traction is more prone to elicit TCR than smooth and gentle traction [1,2,5]. From ocular surgery, several factors are demonstrated to increase the risk of occurrence of TCR: hypercapnia, hypoxemia, light general anesthesia, the stimulus frequency and intensity, and drugs [15,22,24]. Pharmacologic agents such as potent narcotics like sufentanil or alfentanil, beta-blockers, and calcium channel blockers may produce a predisposition to this reflex [1,2,4,5,12,26]. Narcotics may augment vagal tone via their inhibitory action on the sympathetic nervous system. Valid therapeutic maneuvers include the avoidance of factors known to cause predisposition to the reflex, cessation, or modulation of the surgical stimulus. In our cases, mean arterial blood pressure is monitored every five minutes and HR is monitored continuously so the decrease of HR is remarkably observed while blood pressure is stable.

However, risk factors for TCR were compared with results from the literature, but no factor seems to be a predictor of TCR. The risk of TCR in Onyx embolization of DAVFs is 11.1% and early detection and prevention of TCR are necessary. In our series, the incidence of TCR in endovascular treatment with Onyx for DAVFs was 11.11%, which was similar to previous literature reports (10% and 18%) of trans-sphenoidal surgery for pituitary adenomas [21] and microvascular trigeminal de-

compression for trigeminal neuralgia [20]. When stimulation of the trigeminal nerve causes TCR, treatment of hemodynamic instability consists of suspending the procedure and anticholinergic drugs should be administered. Atropine has been shown to effectively extinguish the TCR in our patients. Anticholinergic drugs are not suggested be given prophylactically because they can cause refractory arrhythmias [6]. We did not note a similar reflex with glue or with coils without Onyx. So, in Onyx embolization of DAVFs, patients' ECG should be carefully monitored.

Conclusions

TCR may occur due to chemical stimulus of DMSO and Onyx cast formation, leading to a significant decrease in HR under a standardized anesthetic protocol. We speculate that a slow rate of injection may give DMSO enough time to dissipate in the blood stream and this may be important to prevent toxity. This study confirms that the reflex was blunted by the anticholinergic effects of atropine and there was no harm to patients if stopped immediately.

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