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First Bite Syndrome after Carotid Endarterectomy for High Carotid Bifurcation and Extensive Lesions: Two Case Reports and Literature Review

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Abstract

First bite syndrome (FBS) is an extremely rare complication of carotid endarterectomy (CEA). FBS presents with unique characteristics, development of brief and intense pain in the ipsilateral parotid region at the first bite of each meal, and improvement with subsequent mastication. Here, we report two cases of FBS following CEA. Both cases had anatomical difficulty of a high carotid bifurcation and a high cervical lesion. The lingual and facial arteries (or their common arterial trunk) branched off the external carotid artery (ECA) close to a high carotid bifurcation. The operations required exposure of the ECA distal to these two branches and the distal internal carotid artery (ICA) with a wider range of dissection for clamping the vessels. Several days or weeks after CEA, the patients developed FBS, and their meal-related pain completely resolved in the ensuing weeks. Especially in patients with a high carotid bifurcation, several branches of the ECA tend to originate from the proximal portion of the ECA, similar to octopus arms. During CEA, in these patients, dissection around the ECA and its branches in a wider range is required for exposure of each vessel and placement of the cross-clamp. These procedures can lead to injury to the external carotid nerve and plexus, possibly causing FBS. Additionally, because of the close location of the superior cervical ganglion, external carotid nerves, and distal ICA, manipulation for exposure of the distal end of a high plaque can increase the risk of injury to the cervical sympathetic nerves.

Keywords: carotid artery stenosis, carotid endarterectomy, complication, first bite syndrome, postoperative pain

Introduction

Carotid endarterectomy (CEA) is an established surgical procedure for preventing stroke derived from advanced atherosclerotic carotid artery stenosis.[1,2] Neck dissections in CEA procedures have a potential of iatrogenic injury to cranio-cervical nerves, including the sympathetic system.[3] To date, only eight case reports on first bite syndrome (FBS) related to CEA have been published, and the pathogenic mechanism of FBS secondary to CEA is currently poorly understood because of its rarity.[4-11] FBS is an interesting condition that is rarely observed after upper cervical surgery. In FBS, a brief and sharp pain develops in the parotid region after the first bite of each meal and improves with each bite.[12] The excruciating pain during meals can alter the patients' eating habits and worsen the quality of life. This minor complication of CEA has not been reported in large individual series and clinical trials[1-3] and may be overlooked or under-reported because of misinterpretation.[13] Here, we report two cases of high-grade internal carotid artery (ICA) stenosis with a high carotid bifurcation and a high cervical lesion, which presented with postoperative FBS. We also performed a literature review of this rare complication.

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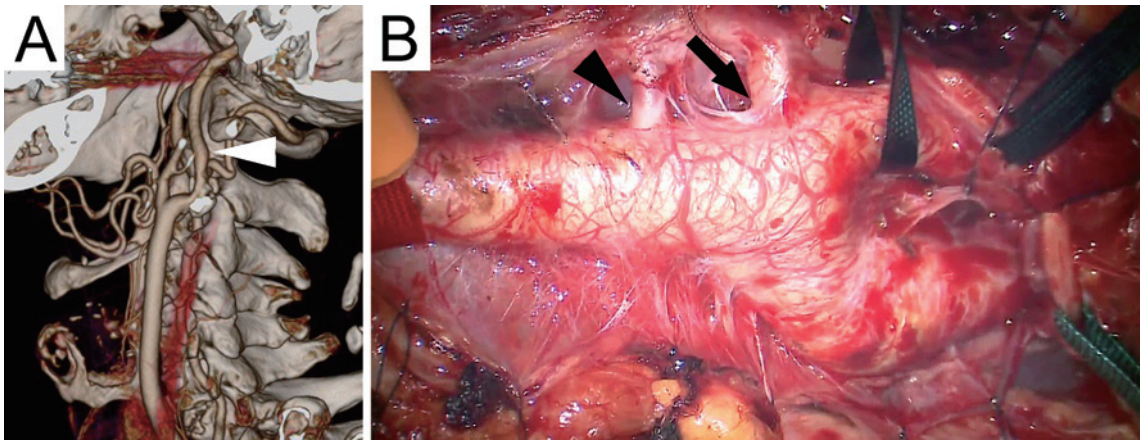

Fig. 1 (A) Three-dimensional reconstruction of preoperative computed tomography angiography showing a high carotid bifurcation and a high cervical lesion. The level of the carotid bifurcation and the distal plaque end (white arrowhead) are located at the C2/3 vertebral body junction and the upper third of the C2 vertebra, respectively. (B) Intraoperative photograph of left carotid endarterectomy. The superior thyroid artery (black arrowhead) and the linguofacial trunk (black arrow) originate from the distal common carotid artery and carotid bifurcation, respectively. Dissection around the origins of the superior thyroid artery, linguofacial trunk, and external carotid artery was performed.

Case Report

Case 1

A 70-year-old man with a history of hypertension, dyslipidemia, and previous CEA for contralateral carotid stenosis suffered from left cerebral infarction. He was diagnosed with artery-to-artery embolism from severe atherosclerotic stenosis at the origin of the left ICA. Computed tomographic angiography showed a high carotid bifurcation and an extensive lesion. The carotid bifurcation was located at the level of the C2/3 vertebral body junction, and the distal end of the plaque was positioned at the upper third of the C2 vertebra (Fig. 1A). Left CEA was performed under general anesthesia. A wide and shallow opening was obtained by using the lift-up method with fishhooks and threads. The hypoglossal nerve was isolated, and the carotid sheath was opened by a linear incision along the carotid arteries. The superior thyroid artery and linguofacial trunk originated from the distal common carotid artery (CCA) and carotid bifurcation, respectively. The origins of the superior thyroid artery, linguofacial trunk, and external carotid artery (ECA) were widely dissected and exposed for cross-clamping to prevent backbleeding during endarterectomy (Fig. 1B). To avoid direct trauma to the nerves, which lay just behind the carotid arteries, circumferential dissection of the vessels was not performed, except for the location where the CCA and the ECA were encircled with vascular loops. Endarterectomy was successfully performed under a microscope with intraluminal shunting. The day after the surgery, a reduced voice range and vocal fatigue were found, but no sharp pain in the periauricular area during meals or signs of Horner's syndrome were observed. On postoperative day 5, he complained of sudden-onset excruciating pain only after the first bite of a meal around the ipsilateral parotid region. The pain rapidly resolved with mastication, but the same pain occurred during each meal. An otorhinolaryngologist team evaluated these symptoms using fiberoptic laryngoscopy and made the diagnosis of FBS without Horner's syndrome and procedure-related injury of the external branch of the superior laryngeal nerve. With conservative management, FBS and the voice conditions completely resolved 3 and 4 weeks later, respectively.

Case 2

A 71-year-old man with a history of hypertension, dyslipidemia, and previous CEA for contralateral carotid artery stenosis was diagnosed with asymptomatic severe atherosclerotic stenosis between the right distal CCA and the origin of the ICA. Cervical angiography of the right CCA showed a high carotid bifurcation located at the level of the upper C3 vertebra, and an extensive lesion reached the level of the middle third of the C2 vertebra (Fig. 2A). Right CEA was performed with the patient under general anesthesia by following the same procedure as that in Case 1. The lingual and facial arteries branched off from the proximal ECA. Therefore, the operation required the exposure of the ECA distal to the lingual and facial arteries for clamping of the vessels (Fig. 2B). After the operation, no neurological deficits were observed. On postoperative day 20, he suddenly presented with sharp pain around the ipsilateral parotid region associated with mastication. This pain occurred at the beginning of a meal for a few seconds and gradually improved with subsequent masticatory movements. We consulted with the otorhinolaryngologist team about this condition, and the pain was diagnosed as postoperative FBS without Horner's syndrome by excluding other causes. Treatment with non-steroidal anti-

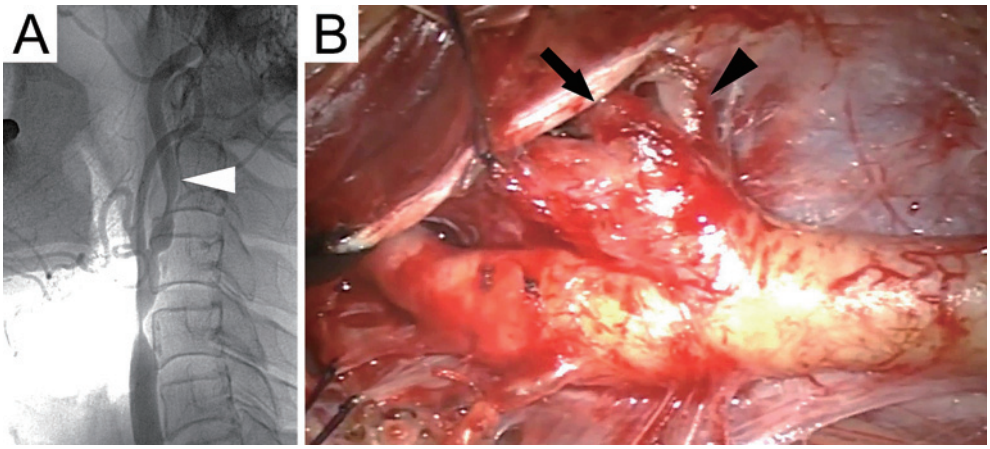

Fig. 2 (A) Lateral view of right preoperative carotid angiography shows a high carotid bifurcation and a high cervical lesion. The carotid bifurcation is located at the level of the C3 vertebra, and the distal plaque end is positioned at the middle third of the C2 vertebra (white arrowhead). (B) Intraoperative photograph of right carotid endarterectomy. The lingual (black arrowhead) and facial (black arrow) arteries branch off from the proximal ECA. Exposure of the ECA distal to the facial artery was obtained for clamping of the vessels. ECA, external carotid artery

inflammatory drugs provided limited relief of the pain, and his clinical symptom completely disappeared 5 weeks after the onset.

Written informed consent was obtained from all patients for publication of this report and the accompanying images.

Discussion

In 1998, Netterville et al. provided the current basis of FBS as a complication associated with surgery for cervical paragangliomas.[14] This basis of FBS was provided after the North American Symptomatic Carotid Endarterectomy Trial and European Carotid Endarterectomy trial, which were the first randomized, controlled trials to evaluate the effectiveness of surgical treatment for carotid artery stenosis.[1,2] Several previous reports established the clinical significance of FBS following infratemporal fossa, parapharyngeal space, or parotid gland tumor surgery, and they showed an incidence of approximately 10%.[12,15,16] FBS has unique characteristics and a unique clinical course. Typically, sharp pain as electric shock in the ipsilateral region of the parotid gland or mandible suddenly occurs at the first bite of a meal. This pain lasts from seconds to minutes, gradually improves as mastication continues, and recurs not only at the following meal but also after a few minutes' break in eating.[12,14,16,17] This symptom characteristically develops within 2 weeks after surgery,[12,16,17] but the onset can vary from immediately to months.[15,16] This pain can be misinterpreted as typical postoperative pain, inflammatory changes, or atypical trigeminal neuralgia.[13,18] Therefore, detailed knowledge of these pain patterns and the latent period of FBS, and repetitive evaluation of meal-related pain, even during the follow-up, are clues to its accurate diagnosis. Although conservative management can relieve this pain for several months, excruciating pain associated with meals significantly impairs the patients' quality of life, even transiently, and the majority of cases remain in partial resolution.[15,16] The optimal treatment for FBS has not been clarified. However, anti-epileptic drugs, including carbamazepine, pregabalin, and gabapentin, tricyclic antidepressants, and intraparotid injection of botulinum toxin type A have been used to mitigate FBS.[16,17]

The pathogenetic mechanisms of FBS have not yet been completely explained. There are complex multifactorial effects on the development of FBS, such as an imbalance in innervation between the sympathetic and parasympathetic nervous systems in the parotid gland, the topographic anatomy of the parapharyngeal space, and damage to the cervical sympathetic system. The sympathetic and parasympathetic nervous systems contribute to myoepithelial cell contraction in the parotid gland. The current theory of the cause of FBS is an imbalance in autonomic nerve innervation between these nervous systems.[18] The denervation of sympathetic nerve branching to the parotid gland due to surgical intervention is assumed to induce parasympathetic cross-stimulation of sympathetic receptors. This denervation results in overcontraction of myoepithelial cells and meal-related pain.[14] However, why the sharp pain occurs, especially in the first bite, and gradually improves with chewing, is unclear. To avoid inadvertent nerve damage causing FBS during CEA, the anatomical knowledge of sympathetic innervation in the neck is essential (Fig. 3). Sympathetic preganglionic fibers destined for distribution to the parotid gland ascend from the thoracic spinal nerves to the neck via the cervical sympathetic trunk and synapse with postganglionic fibers in the superior cervical ganglion (SCG). The cervical sympathetic gan-

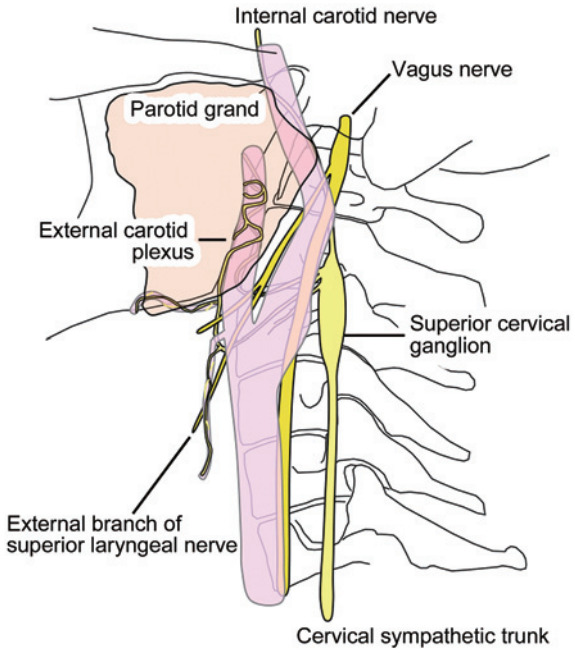

Fig. 3 Schematic illustration of the external carotid nerve and plexus in a case with a high carotid bifurcation. The external carotid nerves originate from the superior part of the superior cervical ganglion, crossing medial to the internal carotid artery, vagus nerve, and ECA, and then run along the ECA and its branches as nerve plexus. ECA, external carotid artery

glion is approximately 3 cm and positioned at the level of C2 and 3, posterior to the carotid sheath, between the ICA and the longus capitis muscle.[12] Postganglionic fibers (i.e., external carotid nerves) leave the superior part of the ganglion, across the distal ICA, and travel directly medial to the ECA with formation of the external carotid plexus within the connective tissue surrounding the ECA. These fibers innervate the parotid grand via the middle meningeal artery plexus.[19] Other postganglionic sympathetic fibers originating from the SCG run along the ICA as the internal carotid nerves and plexus and innervate the eyeball, eyelid, or orbit.[12,20] Therefore, injury of the external carotid nerves and plexus can lead to the occurrence of FBS in the absence of Horner's syndrome, whereas damage to the SCG causes both FBS and Horner's syndrome.[21] Interestingly, not all patients who have injury to the cervical sympathetic trunk develop FBS, which may be caused by residual or autonomous activity of the SCG.[12,14,16,17,20,21] Most of the identified risk factors for postsurgical FBS, such as ECA ligation, sympathectomy, tumor location in the upper neck, and parapharyngeal space dissection, are associated with infratemporal fossa, parapharyngeal space, or parotid gland tumor surgery,[13,15,22] and there are no obvious factors directly related to the CEA procedures, which typically does not involve exposure of these tissues. Table 1 shows a summary of the present cases and eight previous cases of FBS following CEA.[4-11] Of the 10 reported cases, including our cases, 7 showed a high carotid bifurcation or high cervical lesions as the anatomical difficulty in CEA. During CEA, cross-clamping of the ECA is often placed between the superior thyroid artery and the lingual artery. The distance from the carotid bifurcation to the branches of the ECA in cases with a high bifurcation is occasionally shorter than that in cases with non-high bifurcation.[23] Additionally, several branches of the ECA tend to originate from the proximal portion of the ECA similar to octopus arms in these cases. Therefore, dissection around the ECA and its branches in a wider range is required for exposure of each vessel and placement of the cross-clamp in cases with a high bifurcation. Moreover, in patients with high carotid plaques, the distal ICA needs to be accessed, close to where the SCG and external carotid nerves lie. Owing to the location of the SCG and external carotid nerves and plexus, excessive dissection around the ECA and its branches or exposure of the entire extent of high plaques may increase the risk of the injury to sympathetic nerves, resulting in FBS. A total of 349 CEAs were performed at our institute between January 2006 and December 2021. Of the 349 cases, 98 (28.1%) had high cervical lesions, defined as the distal end of the plaque extending above the C2 vertebra.[24] Postoperative FBS was observed in our two cases, with an incidence of 0.6% among all CEA procedures and 2.0% among the cases with high cervical lesions. Japanese people have a significantly higher carotid bifurcation than Western people,[25] which can lead to a high position of the distal end of the carotid plaque. Surgical procedures following CEA with a high carotid bifurcation or high carotid plaques are burdened by technical difficulties, and there is the possibility of serious neurological complications, including craniocervical nerve injury. It is noteworthy that at least half of the cases reporting CEA-related FBS had undergone prior CEA contralateral to the symptom side. However, sympathetic postganglionic fibers innervate unilateral parotid gland as mentioned above. Further consideration will be needed to yield any findings about this feature.

In Case 1, in addition to postoperative FBS, palsy of the external branch of the superior laryngeal nerve was observed. The communicating branch between the SCG and superior laryngeal nerve originates from the SCG as a third branch of the external carotid nerves (Fig. 3). This branch travels posteromedially to the origin of the ECA, to the superior thyroid artery, where it anastomoses with the superior laryngeal nerve. This branch then loops the superior thyroid artery and ascends anterior the ECA until it anastomoses with the external carotid plexus.[19] The superior laryngeal nerve branches from the inferior ganglion of the vagus nerve, crosses medial to the ICA and ECA, and finally divides into the internal branch and external branch close to the superior thyroid artery.[26,27] Damage to the external branch of the superior laryngeal nerve can manifest as ipsilateral paralysis to the cricothyroid muscle, present-

Table 1 Clinical and demographic characteristics of patients who developed first bite syndrome after carotid endarterectomy

Case	Author, year	Age (years)	Sex	Side	Degree of stenosis (%)	Anatomical difficulty for CEA	Prior contralateral CEA	Onset of FBS (post-surgery)	Follow-up of FBS	Clinical outcome of FBS	Other complications
1	Truax, 1989	60	M	Right	80-90	Not applicable	Yes	Hours	1 year	Recovery*	Hypoglossal nerve palsy
2	Albasri, 2011	71	M	Right	Not described	Anatomical difficulty, not described in detail	Not described	Immediately	1 year	Complete recovery	None
3	Wong, 2011	80	M	Left	95-99	High carotid bifurcation, posterior lying ICA	Yes	Days	6 months	Partial recovery	None
4	Wang, 2013	75	M	Right	80-99	High carotid bifurcation	No	2 weeks	1 month	Partial recovery	Vocal cord paralysis
5	Tao, 2016	77	M	Left	95-99	High carotid plaque	Not described	Days	8 months	Complete recovery	None
6	Shiozaki, 2020	67	M	Left	Not described	High carotid plaque	Not described	Days	1 year	Recovery*	None
7	Bikk, 2021	80	M	Right	80	High carotid bifurcation, high carotid plaque, severe ICA tortuosity	Yes	1 week	2 years	Partial recovery	None
8	Charles-Harris, 2021	75	M	Right	>90	Not applicable	No	1 week	6 months	Complete recovery	None
9	Case 1	70	M	Left	75	High carotid bifurcation, high carotid plaque	Yes	5 days	3 weeks	Complete recovery	Superior laryngeal nerve palsy
10	Case 2	71	M	Right	70	High carotid bifurcation, high carotid plaque	Yes	3 weeks	1 month	Complete recovery	None

*The degree of recovery is not described in detail.
CEA, carotid endarterectomy; FBS, first bite syndrome; M, male; ICA, internal carotid artery

ing as hoarseness, vocal weakness, vocal fatigue, or reduced vocal frequency range.[26] Owing to the topographical relationship between the external carotid nerves and the superior laryngeal nerve, manipulation around the superior thyroid artery and the origin of the ECA can cause procedure-related injury of the external carotid nerves and superior laryngeal nerves. To the best of our knowledge, this is the first reported case of both FBS and an external branch of superior laryngeal nerve injury after neck surgery. However, notably, FBS should not be confused with superior laryngeal neuralgia. Superior laryngeal neuralgia is caused by damage to the internal branch of the superior laryngeal nerve, radiating from the thyroid cartilage to the mandibular angle, and occasionally the ear.[28] This paroxysmal pain occurs when swallowing or talking and is triggered by palpation of the superior laryngeal nerve through the thyrohyoid membrane.[28] These pain patterns and trigger point enable differentiation of FBS from superior laryngeal neuralgia.

In conclusion, lesions with high bifurcation and high extension require dissection around the ECA and its branches and the distal ICA. Excessive dissection around the ECA and its branches or around the SCG may result in injury of sympathetic nerves and subsequent FBS. Neurovascular surgeons need to understand the clinical presentation and postoperative time course to avoid overlooking this rare clinical entity. They also need to understand the anatomy of the cervical sympathetic nerve for avoiding in-

advertent damage to the sympathetic system during CEA procedures.

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Abbreviations

CCA, common carotid artery; CEA, carotid endarterectomy; ECA, external carotid artery; FBS, first bite syndrome; ICA, internal carotid artery; SCG, superior cervical ganglion

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Author Contribution

Conception and design: All authors. Drafting the manuscript: Akiyama. Critically revising the manuscript: Hitotsumatsu. Reviewing the submitted version of the manuscript: All authors. Approving the final version of the manuscript on behalf of all authors: Hitotsumatsu. All authors meet the ICMJE authorship criteria.

Conflicts of Interest Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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