JCN Open Access REVIEW

pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2018;14(4):433-443 / https://doi.org/10.3988/jcn.2018.14.4.433

Secondary Short-Lasting Unilateral Neuralgiform Headache with Conjunctival Injection and Tearing: A New Case and a Literature Review

Ya Cao[a*]
Fei Yang[a*]
Zhao Dong[a]
Xusheng Huang[a]
Bingzhen Cao[b]
Shengyuan Yu[a]

[a]Department of Neurology, Chinese PLA General Hospital, Beijing, China
[b]Department of Neurology, General Hospital of Jinan Military Command, Jinan, China

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is a primary headache syndrome with an unclear pathogenesis. However, there is increasing evidence in the literature for secondary SUNCT being attributable to certain known lesions. We explored the possible neurobiological mechanism underlying SUNCT based on all reported cases of secondary SUNCT for which detailed information is available. Here we report a case of neuromyelitis optica spectrum disorders that had typical symptoms of SUNCT that might have been attributable to involvement of the spinal nucleus of the trigeminal nerve. We also review cases of secondary SUNCT reported in the English-language literature and analyze them for demographic characteristics, clinical features, response to treatment, and imaging findings. The literature review shows that secondary SUNCT can derive from a neoplasm, vascular disease, trauma, infection, inflammation, or congenital malformation. The pons with involvement of the trigeminal root entry zone was the most commonly affected region for inducing secondary SUNCT. In conclusion, the neurobiology of secondary SUNCT includes structures such as the nucleus and the trigeminal nerve with its branches, suggesting that some cases of primary SUNCT have underlying mechanisms that are related to existing focal damage that cannot be visualized.

Key Words secondary short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing, systematic short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing, pathogenesis.

INTRODUCTION

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is a primary headache syndrome mentioned in the third part [covering trigeminal autonomic cephalalgias (TACs)] of the International Classification of Headache Disorders, third edition, beta version (ICHD-IIIβ), and is characterized by moderate-to-severe strictly unilateral head pain. The condition is typically characterized by the occurrence of at least 20 attacks lasting 1–600 seconds that involve both ipsilateral conjunctival injection and lacrimation.[1] However, the increasing number of cases of secondary SUNCT attributed to neoplasms, neurovascular compression, infection, inflammation, trauma, and congenital malformations suggests that SUNCT could be a secondary symptom.

Here we report a patient who had SUNCT attributed to demyelination. We also critically review published secondary SUNCT cases for which detailed information from magnetic resonance imaging (MRI) is available up to April 2017, and analyze their etiology and focus location. Through reviewing our own cases and all previously published cases, we aimed

Received January 17, 2018
Revised March 11, 2018
Accepted March 12, 2018

Correspondence
Shengyuan Yu, MD, PhD
Department of Neurology, Chinese PLA General Hospital, Beijing 100853, China
Tel +86-10-55499118
Fax +86-10-88626299
E-mail yusy1963@126.com

*These authors contributed equally to this work.

to summarize the location of lesions that are more likely to induce secondary SUNCT and identify the possible pathogenesis of secondary SUNCT.

METHODS

This study was conducted in two parts: 1) an assessment of a single case from our clinic and 2) a literature review. We defined secondary SUNCT as a SUNCT-like symptom with an etiology corresponding to the diagnosis of SUNCT and secondary headache in ICHD-IIIβ. The literature review was conducted using the online database PubMed. All papers published in English were searched using the terms SUNCT, secondary SUNCT, and systematic SUNCT (last performed in April 2017). References in the discovered papers were also systemically reviewed to identify additional cases published in other articles or abstracts. The inclusion criteria for the literature review were as follows: 1) diagnosis of SUNCT in accordance with ICHD-IIIβ1 and 2) detailed description of competing etiologies or secondary forms of SUNCT such as a neoplasm, vascular disease, or infection. The information extracted for each case included the following: 1) etiology, 2) age at onset, 3) sex, 4) duration, 5) frequency, 6) trigger, 7) pain side, 8) focus location in MRI/CT, and 9) effective treatment.

Some of the cases identified in the literature review might have been included multiple times due to the presence of repeated reports on them without this being indicated.

RESULTS

Case report

A previously healthy 29-year-old male developed paroxysmal vomiting lasting for 2 months, headache, and right-sided visual loss, and began walking unsteadily for approximately 15 days prior to his admission on October 13, 2016. More details of the medical history are provided in Figs. 1–4.

His white blood cell count was 11.17×10^9/L (normal: 3.5–10×10^9/L) and the neutrophil count was 0.736% (normal: 0.50–0.70%), which may have been due to the taking of corticosteroids. A lumbar puncture was performed on October 15. The pressure of the cerebrospinal fluid and its white blood cell count and protein level were 125 mmH_2O, 12×10^6/L

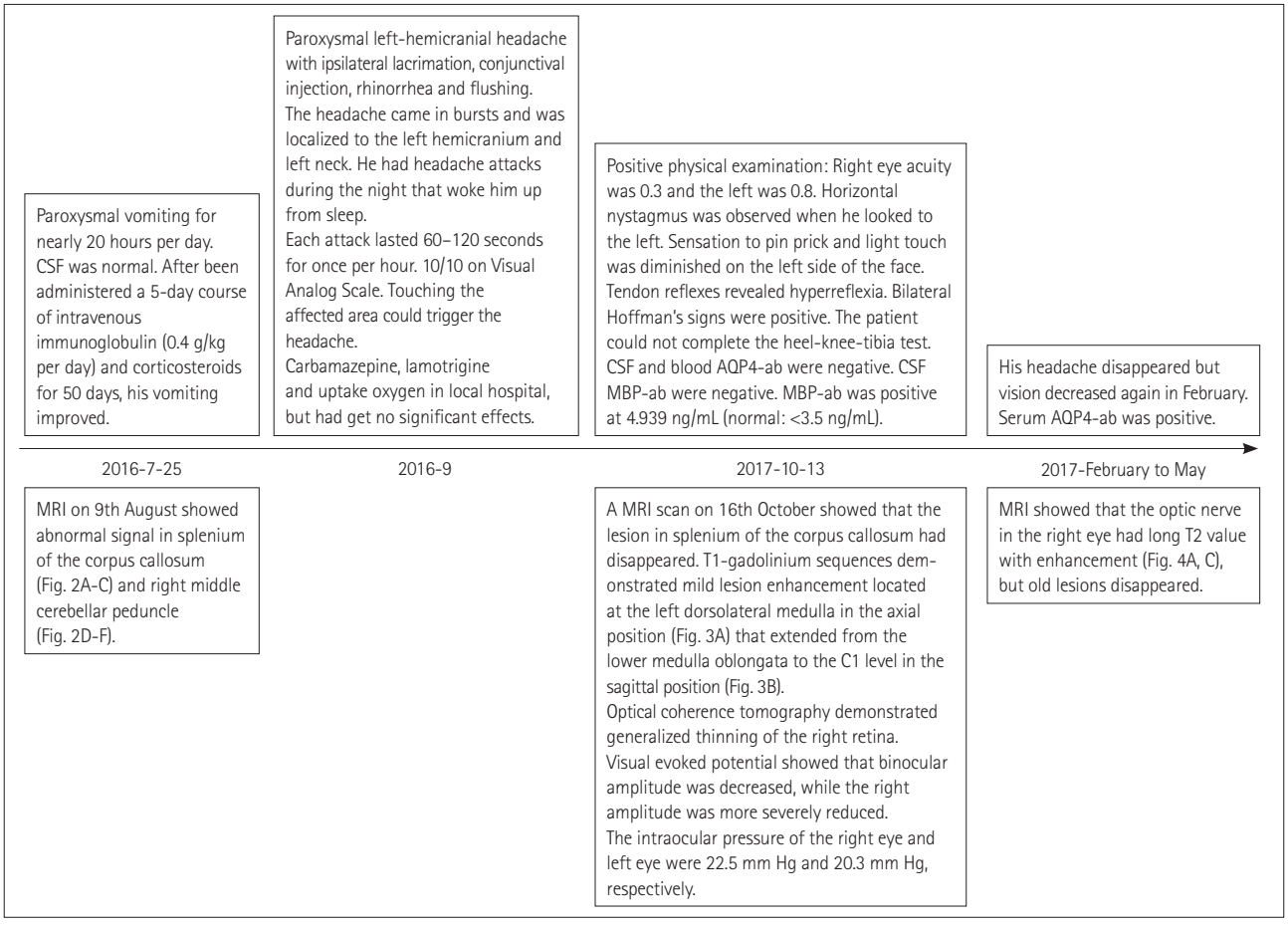

Fig. 1. Medical history. AQP4-ab: aquaporin-4 antibody, CSF: cerebrospinal fluid, MBP-ab: myelin basic protein antibody, MRI: magnetic resonance imaging.

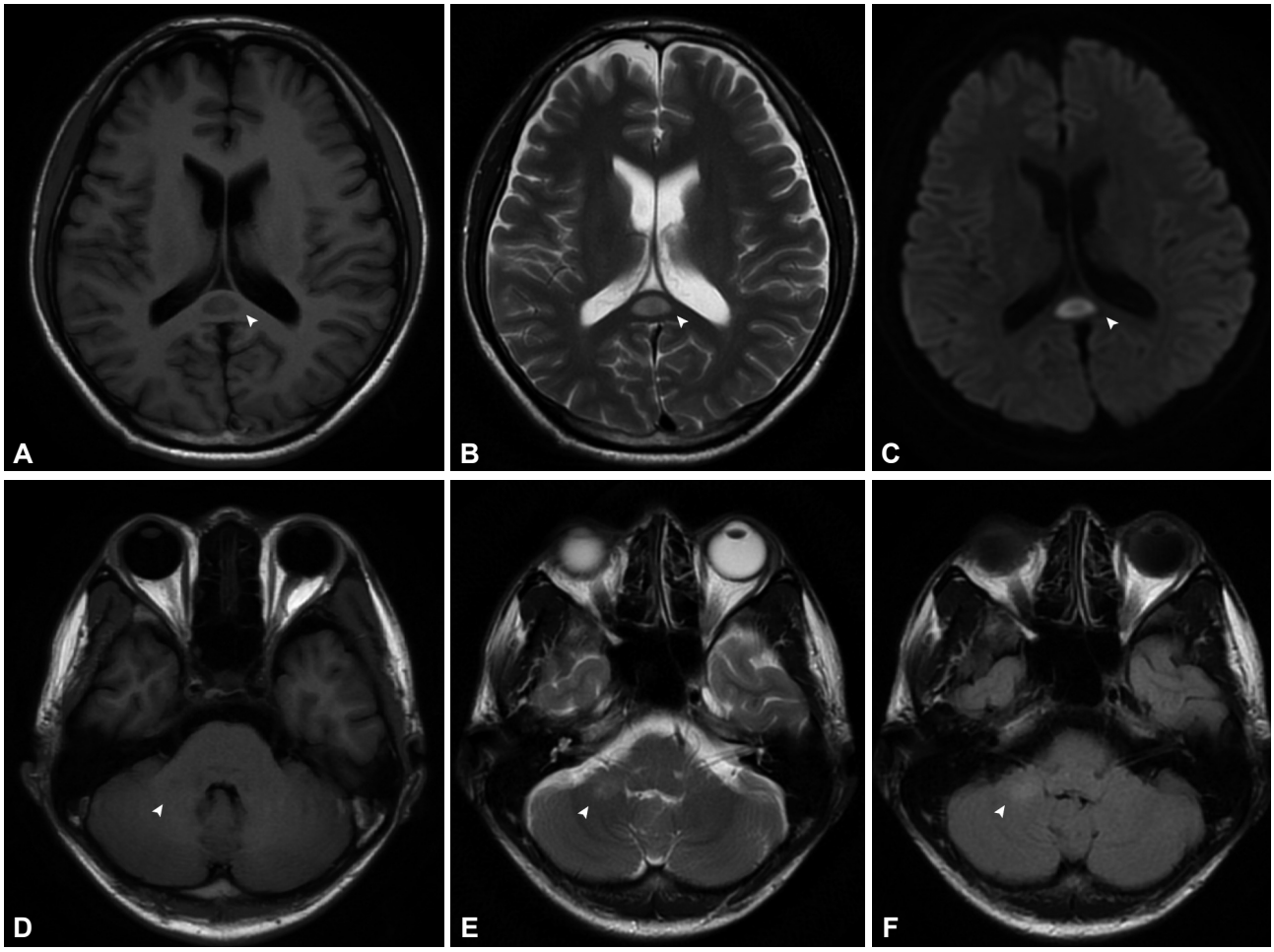

Fig. 2. MRI performed on August 9 showed slightly long T1-weighted (A), and T2-weighted (B) values for the splenium of the corpus callosum (arrowheads) with a high diffusion-weighted-imaging signal (C), and equal T1 signal (D), slightly high T2 (E), and T2 Flair values (F) for the right middle cerebellar peduncle (arrowheads).

(normal: 0–10×10^6/L), and 628.9 mg/dL (normal: 150–400 mg/dL), respectively. The IgG level was 3.89 mg/dL (normal: 0.0–3.4 mg/dL), and no oligoclonal band was detected.

Treatment with 75 mg of oral indomethacin twice daily upon admission to our hospital had little effect. The treatment frequency was reduced slightly to less than once per hour without alleviation of the headache. After excluding tubercular and other infectious diseases, the patient was treated with 1 g of methylprednisolone daily for 3 days and 60 mg of oral prednisolone thereafter. The patient was ultimately diagnosed with SUNCT attributable to demyelination. The paroxysmal hemicranial headaches with autonomic features had ceased 2 days after starting steroid treatment, and his visual acuity had improved to 0.6 in the right eye and 0.8 in the left. The intraocular pressure had decreased to 19.2 mm Hg and 19.7 mm Hg in the right and left eyes, respectively.

His headache had disappeared but his vision was decreased again in February 2017. After performing several examinations we diagnosed neuromyelitis optica spectrum disorders (NMOSD)[2] based on a positive test for serum aquaporin-4 antibody and the presence of standard clinical features of optic neuritis, and attributed his SUNCT-like condition to NMOSD.

Literature review

We summarized 69 cases of SUNCT-like conditions associated with certain etiologies in 62 English-language studies reported on from 1991 to 2017 and for which there were detailed descriptions of the clinical features and imaging results of the patients. These cases comprised 17 with neoplasm,[3-18] 35 with neurovascular disease,[19-43] 2 with trauma,[44,45] 10 with infection,[46-54] 3 with inflammatory disease,[55-57] and 2 with congenital malformation (Table 1, 2, and 3).[58,59]

SUNCT secondary to neoplasm

Eleven of the cases were secondary to pituitary adenoma,[3,7,9-14,16,18] of which four were macroadenoma[3,7,16,18] and three were pituitary microadenoma.[3,9,11] The other six cases

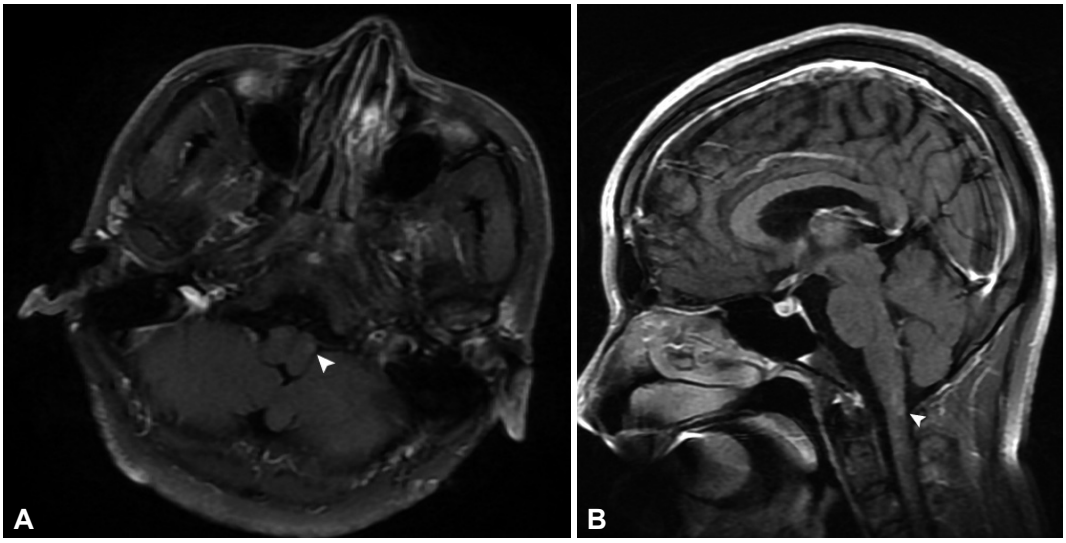

Fig. 3. Enhanced lesion on October 16 located near the left ventral medulla (arrowhead) in axis (A) and extended from the dorsolateral of lower medulla oblongata to the C1 level (arrowhead) in the sagittal position (B).

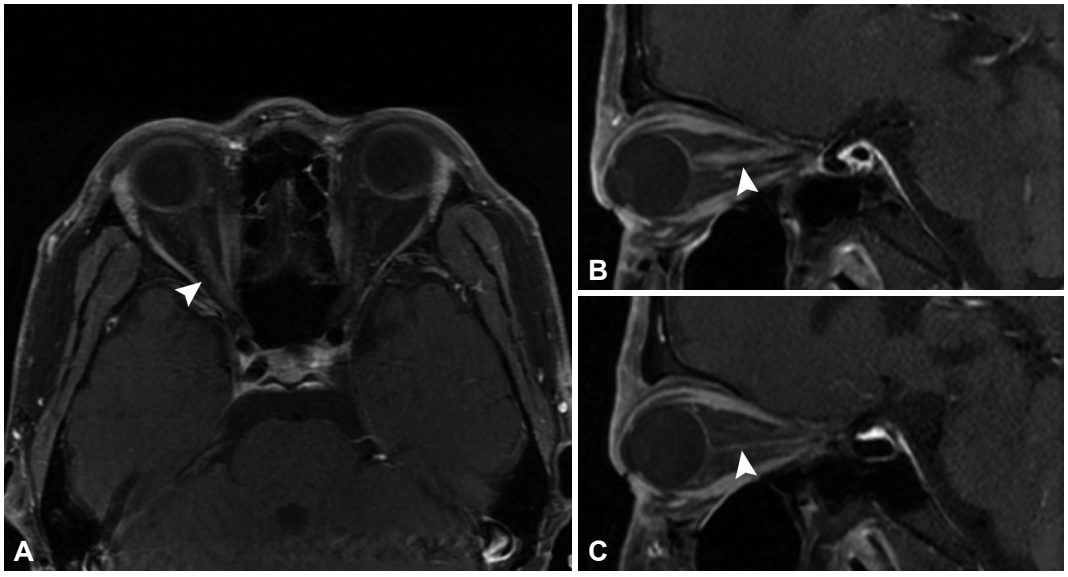

Fig. 4. MRI in May showed the enhanced lesion in the optic nerve (arrowheads) of the right eye (A and B), while the left side was normal (C).

comprised leiomyosarcoma,[5] pilocytic astrocytoma,[4] epidermoid tumor,[17] cyst,[6] pulmonary metastases,[8] and meningioma.[15] MRI findings showed that five cases were located in the cavernous sinus, two in the pons, two in the ocular region, two in the carotid artery, and one in the frontotemporal area. Another six cases comprising three pituitary microadenomas and three pituitary adenomas showed no extension in MRI.

SUNCT secondary to neurovascular disease

Thirty cases were caused by neurovascular compression,[19,20,22,24-28,30-36,39-43] four cases were due to cerebral infarction,[23,29,37,38] and one case was due to cavernous angioma.[21] MRI findings showed that 32 cases were at the pons level, including a case of left cerebellar infarction, while its ischemic penumbra was considered to involve the ascending spinothalamic tract and descending trigeminal fibers at or below their site of entry (and subsequent caudal passage) into the lateral pontine tegmentum. Three cases were located in the unilateral dorsolateral medulla with the possible involvement of the spinal nucleus of the trigeminal nerve.

SUNCT secondary to other etiologies

The cases with other etiologies showed scattered focus locations. The trauma areas included head and whiplash injuries. The infection areas covered the chronic sinusitis, eth-

Table 1. Clinical features of 17 patients with short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing attributed to neoplasm

Disease	Patient no.	Age at onset (years)	Sex	Duration (seconds)	Frequency (per day)	Trigger	Pain side	Focus location in MRI/CT	Effective treatment
Pituitary macroadenoma	1[7]	26	M	20–30	1–6	Yes	R	R cavernous sinus and carotid artery	BCT
	2[16]	33	M	10	1–10	Yes	L	L cavernous sinus	DA
	3[18]	35	F	60–120	40	Yes	R	R cavernous carotid artery	LMT
	4[3]	27	F	15–30	N/A	Yes	L	L cavernous sinus	Radiotherapy
Pituitary adenoma	5[13]	46	M	15–120	3–6	Yes	L	L cavernous sinus	CAB
	6[12]	22	F	<60	5–10	Yes	L	No extension	CAB
	7*[10]	26	M	60	2–8	N/A	L	No extension	Surgery
	8[14]	18	F	30	5–10	No	B	No extension	LMT
Pituitary microadenoma	9[3]	24	F	15–30	10–30	Yes	L	No extension	Surgery
	10[9]	28	M	20–30	100–200	N/A	R	No extension	Surgery
	11[11]	33	M	60–120	30	N/A	L	No extension	Surgery
Leiomyosarcoma	12[5]	45	M	60–120	10–15	Yes	L	L cavernous sinus	N/A
Pilocytic astrocytoma	13[4]	11	F	30–60	20	No	R	R pons–CPA	Surgery
Epidermoid tumor	14[17]	33	M	30–60	240	Yes	L	L pons–CPA	Surgery
Cyst	15[6]	23	F	10–60	20–30	Yes	R	R ocular region	Surgery
Pulmonary metastases	16[8]	69	F	60–120	50–70	Yes	R	R ocular region	Radiotherapy
Meningioma	17[15]	81	F	N/A	60	No	L	L frontotemporal infiltrative growing	GBP

*Nonfunctioning adenoma.
BCT: bromocriptine, CAB: cabergoline, CPA: cerebellopontine angle, CT: computed tomography, DA: dopamine, GBP: gabapentin, LMT: lamotrigine, MRI: magnetic resonance imaging, N/A: not applicable.

moid sinusitis, sphenoiditis, and orbital venous vasculitis, and included two cases of viral meningitis/meningoencephalitis and three of varicella-zoster virus infection. Inflammation included one case of neuromyelitis optica and two cases of multiple sclerosis, both of which were due to congenital malformation with skull abnormalities.

Focus location

According to the etiology classification (Table 4), the most common location of the neoplasm was the cavernous sinus (5/18), followed by the pons, ocular region, and carotid artery (each 2/18), and then the frontotemporal area (1/18). Moreover, another six cases of pituitary adenoma showed no extension out of the sellar space, one of which was a nonfunctioning adenoma associated with headaches that ceased after surgery or administering cabergoline. In cases with vascular disease, the pons (32/35) and medulla (3/35) were common locations at which SUNCT was induced. Six of the ten cases of infectious disease and both traumatic cases showed no abnormalities in imaging, while the focus in the other four cases of infection was in the cervical spinal cord, ocular region, maxillary sinus, and sphenoid sinus. Since the focal lesions were scattered throughout demyelinated areas, we only focused on the most likely locations such as the pons, medulla, and cervical spinal cord (two cases), and the ocular region (one case). The focal lesions were difficult to locate in the two cases of congenital malformation due to skull abnormalities, but the most likely location was the pons in both cases.

According to the classification of focus location (Table 5), the pons was the most common location where SUNCT-like syndrome was induced, and 32 cases were vascular diseases while 6 involved neoplasms, demyelination, and congenital malformations. The second most common locations were the medulla and cavernous sinus, each comprising five cases. The medulla accounted for three cases of vascular disease and two cases of demyelination, and the cavernous sinus was only involved in cases of neoplasm. The third and fourth most common locations were the ocular region (two cases with neoplasm and two with infection or demyelination) and cervical spinal cord (two cases with demyelination and one with infection), respectively. The carotid artery (two cases of neoplasm), frontotemporal area (one case of neoplasm), maxillary sinus (one case of infection), and sphenoid sinus (one case of infection) were less common locations. In addition, no lesions were detected in imaging investigations in six cases of infection and two of trauma, but two cases of infection showed narrowing of the superior ophthalmic vein and a higher temperature around the ipsilateral orbital region. Finally, the tumor did not extend to

Table 2. Clinical features of 35 patients with short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing attributed to vascular disease

Disease	Patient no.	Age at onset (years)	Sex	Duration (seconds)	Frequency (per day)	Trigger	Pain side	Focus location in MRI/CT	Effective treatment
Neurovascular compression	18[19]	33	M	30	360	No	L	L pons–CPA–arteriovenous malformation	CBZ
	19[20]	55	M	30	280–360	Yes	R	R pons–CPA–vascular malformation	CBZ, AMT
	20[22]	43	F	30–45	6–7	Yes	R	R pons–PCC–SCA	MVD
	21[25]	54	F	60–120	N/A	Yes	L	L pons–PCC–SCA	MVD
	22[26]	47	M	60	30–40	Yes	R	R pons–PCC–SCA	MVD
	23[33]	67	M	1–60	<720	Yes	R	R pons–PCC–SCA	DBS
	24[34]	45	F	Seconds	20–60	Yes	L	L pons–PCC–SCA	MVD
	25[36]	44	M	30–60	>20	Yes	R	R pons–PCC–SCA	OXA, LMT
	26[30]	57	M	30–120	120–240	N/A	L	L pons–PCC–SCA VL	MVD
	27[31]	54	M	5–10	3–10	Yes	L	L pons–PCC–SCA VL	MVD
	28[32,40]	65	F	60–180	30–200	Yes	R	R pons–PCC–SCA VL	MVD
	29[32]	65	M	60–120	30–200	Yes	R	R pons–SCA	N/A
	30[32,40]	43	M	30–120	20–30	No	L	L pons–AICA	LMT, lignocaine
	31[32,40]	46	F	3–10	90–120	Yes	R	R pons–SCA	LMT, lignocaine
	32[32]	44	F	30–120	100–300	Yes	N/A	Pons–SCA	N/A
	33[32,40]	19	M	20–180	8–10	Yes	L	L pons–SCA	LMT
	34[35]	60	M	20–30	20–50	Yes	R	R pons–PCC–SCA VL	OXA, LMT
	35[35]	55	M	10–90	25–30	Yes	R	R pons–SCA VL	LMT
	36[35]	64	M	10–30	5–30	Yes	R	B pons–SCA VL	CBZ
	37[36]	46	M	30–60	1–6	Yes	R	R pons–SCA VL	CBZ, IM
	38[36]	50	F	2–180	>100	Yes	R	R pons–SCA VL	MVD
	39[24]	48	M	20–30	15–20	Yes	L	L pons–AICA	None
	40[27]	68	M	60–120	3–7	N/A	L	L pons–BA VL	GBP
	41[28]	55	M	30	20–30	No	L	L pons–vertebrobasilar	None
	42[39]	52	M	360	N/A	Yes	R	R pons–PCC–VA	MVD
	43[39]	65	M	Seconds	N/A	N/A	R	R pons–PCC–SCA, AICA	MVD
	44[41]	46	F	60–120	N/A	Yes	R	R pons–PCC–SCA	MVD
	45[41]	69	F	120–180	N/A	Yes	R	R pons–PCC–SCA	CBZ
	46[42]	43	F	30–45	6–7	Yes	R	R pons–SCA	MVD
	47[43]	40	F	<300	2–30	Yes	R	R pons–SCA	LMT, GBP, amitriptyline
Cerebellar infarction	48[23]	63	M	20–180	8	Yes	L	L pons–ischemic–penumbra of cerebellar	N/A
	49[29]	54	M	20	10	No	R	R dorsolateral medulla	None
	50[37]	64	M	3–10	1–4	No	L	L dorsolateral medulla	N/A
	51[38]	58	M	20	12–15	Yes	R	R dorsolateral medulla	CBZ, GBP
Cavernous angioma	52[21]	60	M	60	15–23	N/A	L	L pons	CBZ

AICA: anterior inferior cerebellar artery, AMT: amitriptyline, BA: basilar artery, CBZ: carbamazepine, CPA: cerebellopontine angle, CT: computed tomography, DBS: deep brain stimulation, GBP: gabapentin, IM: indomethacin, LMT: lamotrigine, MRI: magnetic resonance imaging, MVD: microvascular decompression, N/A: not applicable, OXA: oxcarbazepine, PCC: pontocerebellar cistern, SCA: superior cerebellar artery, VA: vertebral artery, VL: vascular loop.

adjacent tissues in six cases of pituitary adenoma.

DISCUSSION

SUNCT is a primary headache classified as a TAC.[1] However, increasing numbers of SUNCT cases with known etiology have been reported. The case included in the present study was diagnosed as secondary SUNCT since it fulfilled the ICHD-IIIβ diagnostic criteria for SUNCT and was attributable to NMOSD,[2] which is a rare cause that has seldom been reported previously. The case with a left-sided headache had lesions on the contralateral cerebellopontine angle (CPA) and ipsilateral medulla. However, the lesion on the CPA appeared at least 2 months before the onset of the head-

Table 3. Clinical features of 17 patients with short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing attributed to other etiologies

Disease	Patient no.	Age at onset (years)	Sex	Duration (seconds)	Frequency (per day)	Trigger	Pain side	Focus location in MRI/CT	Effective treatment
Head injury	53[44]	20	M	20–60	160	Yes	R	None	CBZ
Whiplash injury	54[45]	62	F	120–240	40–50	Yes	R	None	GON blocks
Sinusitis	55[47]	53	M	5–10	144	Yes	L>R	B maxillary sinuses	FESS
Ethmoid sinusitis	56[49]	71	M	3–5	>100	N/A	R	R ocular region	FESS
Sphenoiditis	57[52]	62	F	60–240	>20	N/A	R	R sphenoid sinus	AMX–clavulanate
Orbital venous vasculitis	58[46]	49	M	300–600	1–180	Yes	R	None*	Steroids, AZA
Viral meningitis	59[50]	49	M	10	100–200	N/A	R	None†	Sumatriptan
VZV meningoencephalitis	60[48]	46	F	30–60	240	No	R	None‡	VPA
	61[53]	72	M	10–60	20–40	Yes	R	None‡	GBP
VZV	62[54]	58	M	20	96–120	Yes	R	None	Pregabalin, LMT
	63[54]	60	M	10–60	120	N/A	L	None	Pregabalin
	64[51]	57	F	5–30	50–100	No	L	Cervical spinal cord (C2/C3, C5/C6)	GBP
NMO	65[55]	41	F	10–15	20	N/A	L>R	Medulla to cervical spinal cord (C6); ocular region	MP, IVIg
MS	66[56]	18	M	5–30	20	N/A	R	R medulla; pons; cervical spinal cord.	N/A
	67[57]	59	F	Seconds	720	N/A	L	L pons	Steroids, CMZ, IM
Osteogenesis imperfecta	68[58]	42	M	120–180	1–5	Yes	L	Basilar impression; L pons	CBZ
Craniosynostosis brachycephaly	69[59]	14	F	60	50	Yes	R	Foreshortened posterior fossa; more notable in the R pons–CPA	CBZ, PDN, lithium carbonate

*Narrowing of superior ophthalmic vein, †Thermogram showed that the skin temperature was higher around the orbital region than around the left side, suggesting decreased right sympathetic nerve function, ‡CT scans were normal when headache started. The author considered them to be a peripheral mechanism.
AMX: amoxicillin, AZA: azathioprine, CBZ: carbamazepine, CMZ: carbimazole, CPA: cerebellopontine angle, CT: computed tomography, FESS: functional endoscopic sinus surgery, GBP: gabapentin, GON: greater occipital nerve, IM: indomethacin, IVIg: intravenous immunoglobulin, MP: methylprednisolone, MRI: magnetic resonance, MS: multiple sclerosis, N/A: not applicable, NMO: neuromyelitis optica, PDN: prednisone, VPA: valproic acid, VZV: varicella-zoster virus.

ache, and so we considered the lesion on the dorsolateral medullar to be the one responsible. Moreover, we summarized the focus locations of 69 cases that met the ICHD-IIIβ diagnosis criteria for SUNCT and were attributed to neoplasms, vascular disease, trauma, infection, inflammation, and congenital malformations, indicating that secondary SUNCT indeed exists. The exact pathogenesis of secondary SUNCT has not yet been well established, but our findings have revealed that there are certain main areas where SUNCT is induced.

The probable SUNCT-related trigeminal nerve conduction pathway[60] is illustrated as follows (Fig. 5): First, the afferent pathways (sensory fibers) comprising the primary neurons of the trigeminal nerve are located in the trigeminal ganglion, with peripheral processes distributed among the head and facial, skin, oral, and nasal mucosa receptors. After entering the pons, nociceptive afferents of the central process terminate in subnuclei of the trigeminal brainstem nuclear complex. Some of the fibers of the secondary neurons in the nuclear complex and the gray matter of upper cervical spinal cord segments (C1 to C2) form the trigeminohypothalamic tract[61] and then project to or go through the hypothalamus. The other fibers from the sensory and spinal nucleus of the trigeminal nerve cross upward, and the composite trigeminal lemniscus terminates in the ventral posteromedial nucleus of the thalamus, passing the posterior limb of the internal capsule and ending at the postcentral gyrus. Second, the efferent pathways (motor fibers) in the hypothalamus regulate lachrymal gland secretion. Parasympathetic fibers of the facial nerve are sent out by the superior salivatory nucleus and terminate in the pterygopalatine ganglion via the greater petrosal nerve. Postganglionic fibers of the pterygo-

Table 4. Distribution of lesion locations according to the etiology classification

Variable	*n* (%)
Neoplasm (*n*=18)	
No extension	6 (33.33)
Cavernous sinus	5 (27.78)
Pons	2 (11.11)
Ocular region	2 (11.11)
Carotid artery	2 (11.11)
Frontotemporal area	1 (5.56)
Vascular disease (*n*=35)	
Pons	32 (91.43)
Medulla	3 (8.57)
Trauma (*n*=2)	
None	2 (100)
Infection (*n*=10)	
None	6 (60)
Maxillary sinus	1 (10)
Ocular region	1 (10)
Sphenoid sinus	1 (10)
Cervical spinal cord	1 (10)
Demyelination* (*n*=3)	
Pons	2 (66.67)
Medulla	2 (66.67)
Cervical spinal cord	2 (66.67)
Ocular region	1 (33.33)
Congenital malformation (*n*=2)	
Pons	2 (100)

*Demyelination had multiple focuses, each of which could be the lesion responsible for inducing short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing.

Table 5. Distribution of etiology according to the classification of lesion location

Location	*n* (%)
Pons (*n*=38)	
Vascular disease	32 (84.22)
Neoplasm	2 (5.26)
Demyelination	2 (5.26)
Congenital malformation	2 (5.26)
Medulla (*n*=5)	
Vascular disease	3 (60)
Demyelination	2 (40)
Cavernous sinus (*n*=5)	
Neoplasm	5 (100)
Ocular region (*n*=4)	
Neoplasm	2 (50)
Infection	1 (25)
Demyelination	1 (25)
Cervical spinal cord (*n*=3)	
Demyelination	2 (66.67)
Infection	1 (33.33)
Carotid artery (*n*=2)	
Neoplasm	2 (100)
Frontotemporal area (*n*=1)	
Neoplasm	1 (100)
Maxillary sinus (*n*=1)	
Infection	1 (100)
Sphenoid sinus (*n*=1)	
Infection	1 (100)
None (*n*=8)	
Infection	6 (75)
Trauma	2 (25)
No extension (*n*=6)	
Neoplasm	6 (100)

palatine ganglion are distributed to the mucous membrane in the lachrymal gland, palate, and nosepiece, controlling the exudation of the mucous membrane and gland body.

Based on the conduction pathway and images in the literature, we assumed that three areas were mainly responsible for the induction of secondary SUNCT (Fig. 5): 1) the dorsolateral medulla and upper cervical spinal cord where the spinal nucleus of the trigeminal nerve is located (Shadow A in the Fig. 5), 2) the pons (Shadow B) in which vascular compression was likely to occur, and 3) the preganglionic fibers of the trigeminal nerve (Shadow C) that was the focus of neoplasm and widespread infection. Cases with cerebral infarction,[23,29,37,38] infection,[51] and demyelination[55,56] explicitly manifested in the Shadow-A area because they mainly exhibited lesions in the pons, dorsolateral medulla, and cervical spinal cord (C1 to C2) where the trigeminal divisions, trigeminal nucleus, spinothalamic tract, and trigeminohypothalamic tract are present and thus induce SUNCT. Neurovascular compression[19,20,22,24-28,30-36,39-43] was the most common reason in cases in the Shadow-B area, which could be clearly visualized using MRI and could accurately indicate vascular malformation in the CPA cistern that involves the trigeminal root entry zone and mostly irritates fibers of the first division (V1) of the trigeminal nerve and the greater petrosal nerve; thus, patients would present with accompanying conjunctival injection and tearing. However, there were more than 35 cases of neurovascular compression in our review. Williams and Broadley,[40] Sebastian et al.[60] and Favoni et al.[36] reported other cases of SUNCT secondary to neurovascular compression that were excluded from our review due to a lack of detailed information.

In addition, there were focuses in the lateral cavernous sinus, frontotemporal region, maxillary sinus, sphenoid sinus, ocular region, and carotid sinus, and six cases of infection showed no abnormities on MRI/CT, while two of the

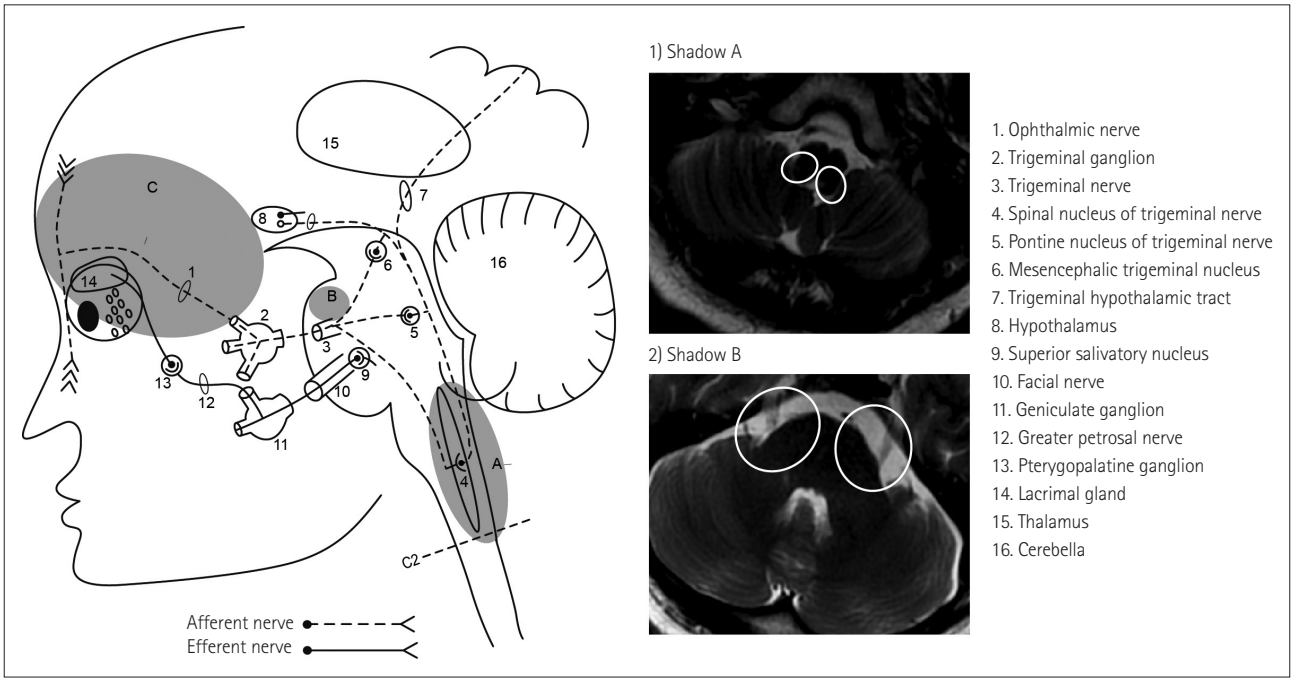

Fig. 5. Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing-related pathways and structures. Shadow A represents the dorsolateral medulla and upper cervical spinal cord where the spinal nucleus of the trigeminal nerve was located, which was often affected by cerebral infarction and demyelination. Vascular compression was likely to occur in the area of Shadow B. The neoplasm and infection had a widespread focus, and were mostly located at the preganglionic fibers of the trigeminal nerve (Shadow C).

cases exhibited narrowing of the superior ophthalmic vein[46] and a higher temperature around the ipsilateral orbital region.[50] These cases also have a high probability of developing invasion into the divisions of the trigeminal nerve because the focus of the neoplasm and infection can sometimes invade the intracranial and extracranial structures associated with pain sensitivity. These include the endocranium and divisions of the trigeminal nerve (frontal, lachrymal, and nasociliary nerves of the ophthalmic, maxillary, and mandibular nerves) that cannot be seen clearly in images, which was inevitably the actual causal lesion for secondary SUNCT. However, six cases of pituitary adenoma showed a focus in the sellar region without extending to the adjacent tissue. These cases comprised three of microadenoma, another three for which the tumor size was not stated explicitly, and one that was a nonfunctioning tumor. Although the pathophysiology of pituitary-associated headache is not well understood, and most authors have suspected it to be related to abnormalities in the hypothalamic-pituitary endocrine system, we still primarily attributed the effect to unseen cadaverous sinus invasion, dural stretching, or local pressure effects because the nonsecreting tumor case[10] represented negative evidence that SUNCT-like headaches can also occur when hormone levels are normal. In other words, pain in the V1 area may to some extent arise from pressure or stretching of the first division of the trigeminal nerve adjacent to the cavernous sinus, whereas other nerves such as the oculomotor, trochlear, and abducent nerves will be not involved due to the limitations of the pressure.

Regarding the associated symptoms such as conjunctival injection and tearing, we inferred that the lesions indicated by Shadows B and C in Fig. 5 had mostly invaded the first division of the trigeminal nerve with distribution of the parasympathetic nerve fiber in the mucous membrane in the lachrymal gland. However, due to the conduction pathway being unknown, we only determined that the trigeminal autonomic symptoms were related to the salivary nucleus and could not elucidate how lesions in Shadow-A areas could induce conjunctival injection and tearing.

Our search of the references revealed that the secondary causes for SUNCT can also reportedly cause trigeminal neuralgia and other TACs. For example, vascular compression can induce short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms-like headache[36] that is associated with conjunctival injection or lacrimation. Chiari malformation type I,[62] focal cervical myelitis,[63] diffuse large-B-cell lymphoma of the nasopharynx,[64] and upper cervical meningioma[65] can induce cluster-like headache, whose lesions were similar to those of SUNCT. Although our extensive literature search did not reveal a feasible mechanism to indicate the difference, we speculate that affected anatomical structures are the main reason.

Secondary SUNCT will occur with damage to the nucleus, tracts, and peripheral nerves, and the possibility of secondary symptoms cannot be excluded in primary cases with normal imaging findings because some focal damage cannot be visualized using current imaging methods. We have illustrated that certain aspects of SUNCT might be a secondary symptom. When encountering patients with SUNCT in the clinical situation, the best option for physicians is to perform MRI scans with high-resolution sequences of basal cisterna and pituitary fossa sections .

CONCLUSIONS

We have presented a special case of secondary SUNCT with demyelination. We also reviewed all reported cases of secondary SUNCT in the English-language literature since this condition was first reported in 1991, and analyzed its etiology, focus location, and pain laterality. Finally, we hypothesized three mechanisms for secondary SUNCT and assumed that some aspects of this condition might be a secondary symptom, although some lesions cannot be visualized.

Conflicts of Interest

The authors have no financial conflicts of interest.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (grants 81471147, 81671077, 81471146, 81500966, 81500943, and 81600952), Beijing Science and Technology Project (grant Z16110000 2616013), the Capital Development Scientific Research (grant 2014-4-5013), and Beijing Natural Science Foundation (grant 7162178).

REFERENCES

1. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition (beta version). *Cephalalgia* 2013;33:629-808.
2. Tan CT, Mao Z, Qiu W, Hu X, Wingerchuk DM, Weinshenker BG. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology* 2016;86:491-492.
3. Massiou H, Launay JM, Levy C, El Amrani M, Emperauger B, Bousser MG. SUNCT syndrome in two patients with prolactinomas and bromocriptine-induced attacks. *Neurology* 2002;58:1698-1699.
4. Blättler T, Capone Mori A, Boltshauser E, Bassetti C. Symptomatic SUNCT in an eleven-year-old girl. *Neurology* 2003;60:2012-2013.
5. Kaphan E, Eusebio A, Donnet A, Witjas T, Chérif A. Shortlasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing (SUNCT syndrome) and tumour of the cavernous sinus. *Cephalalgia* 2003;23:395-397.
6. Lim EC, Teoh HL. Headache - it's more than meets the eye: orbital lesion masquerading as SUNCT. *Cephalalgia* 2003;23:558-560.
7. Matharu MS, Levy MJ, Merry RT, Goadsby PJ. SUNCT syndrome secondary to prolactinoma. *J Neurol Neurosurg Psychiatry* 2003;74:1590-1592.
8. Black D, Swanson J, Eross E, Cutrer FM. Secondary SUNCT due to intraorbital, metastatic bronchial carcinoid. *Cephalalgia* 2005;25:633-635.
9. Leroux E, Schwedt TJ, Black DF, Dodick DW. Intractable SUNCT cured after resection of a pituitary microadenoma. *Can J Neurol Sci* 2006;33:411-413.
10. Rocha Filho PA, Galvão AC, Teixeira MJ, Rabello GD, Fortini I, Calderaro M, et al. SUNCT syndrome associated with pituitary tumor: case report. *Arq Neuropsiquiatr* 2006;64:507-510.
11. Rozen TD. Resolution of SUNCT after removal of a pituitary adenoma in mild acromegaly. *Neurology* 2006;67:724.
12. Jiménez Caballero PE. SUNCT syndrome in a patient with prolactinoma and cabergoline-induced attacks. *Cephalalgia* 2007;27:76-78.
13. de Lourdes Figuerola M, Bruera O, Pozzo MJ, Leston J. SUNCT syndrome responding absolutely to steroids in two cases with different etiologies. *J Headache Pain* 2009;10:55-57.
14. Zidverc-Trajkovic J, Vujovic S, Sundic A, Radojicic A, Sternic N. Bilateral SUNCT-like headache in a patient with prolactinoma responsive to lamotrigine. *J Headache Pain* 2009;10:469-472.
15. Kutschenko A, Liebetanz D. Meningioma causing gabapentin-responsive secondary SUNCT syndrome. *J Headache Pain* 2010;11:359-361.
16. Musuka TD, Edis RH, Kermode AG. Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing caused by a pituitary adenoma. *J Clin Neurosci* 2013;20:1180-1181.
17. Rodgers SD, Marascalchi BJ, Strom RG, Huang PP. Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing syndrome secondary to an epidermoid tumor in the cerebellopontine angle. *Neurosurg Focus* 2013;34:E1.
18. Berk T, Silberstein S. Case report: secondary SUNCT after radiation therapy--a novel presentation. *Headache* 2016;56:397-401.
19. Bussone G, Leone M, Dalla Volta G, Strada L, Gasparotti R, Di Monda V. Short-lasting unilateral neuralgiform headache attacks with tearing and conjunctival injection: the first "symptomatic" case? *Cephalalgia* 1991;11:123-127.
20. Morales F, Mostacero E, Marta J, Sanchez S. Vascular malformation of the cerebellopontine angle associated with "SUNCT" syndrome. *Cephalalgia* 1994;14:301-302.
21. De Benedittis G. SUNCT syndrome associated with cavernous angioma of the brain stem. *Cephalalgia* 1996;16:503-506.
22. Gardella L, Viruega A, Rojas H, Nagel J. A case of a patient with SUNCT syndrome treated with Jannetta procedure. *Cephalalgia* 2001;21:996-999.
23. Penart A, Firth M, Bowen JR. Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) following presumed dorsolateral brainstem infarction. *Cephalalgia* 2001;21:236-239.
24. Köseoglu E, Karaman Y, Kücük S, Arman F. SUNCT syndrome associated with compression of trigeminal nerve. *Cephalalgia* 2005;25:473-475.
25. Lagares A, Gómez PA, Pérez-Nuñez A, Lobato RD, Ramos A. Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing syndrome treated with microvascular decompression of the trigeminal nerve: case report. *Neurosurgery* 2005;56:E413.
26. Sprenger T, Valet M, Platzer S, Pfaffenrath V, Steude U, Tolle TR. SUNCT: bilateral hypothalamic activation during headache attacks and resolving of symptoms after trigeminal decompression. *Pain* 2005;113:422-426.
27. Zidverc-Trajkovic J, Mijajlovic M, Pavlovic AM, Jovanovic Z, Sternic N. Vertebral artery vascular loop in SUNCT and concomitant trigeminal neuralgia. case report. *Cephalalgia* 2005;25:554-557.
28. Mondéjar B, Cano EF, Pérez I, Navarro S, Garrido JA, Velásquez JM, et al. Secondary SUNCT syndrome to a variant of the vertebrobasilar vascular development. *Cephalalgia* 2006;26:620-622.
29. Rodrigues GG, Bordini CA, Dach F, Eckeli A, Speciali JG. SUNCT syndrome: report of a possible symptomatic case. *Arq Neuropsiquiatr* 2007;65:852-854.
30. Guerreiro R, Casimiro M, Lopes D, Marques JP, Fontoura P. Video NeuroImage: symptomatic SUNCT syndrome cured after trigeminal

neurovascular contact surgical decompression. *Neurology* 2009;72:e37.
31. Irimia P, González-Redondo R, Domínguez PD, Díez-Valle R, Martínez-Vila E. Microvascular decompression may be effective for refractory SUNCT regardless of symptom duration. *Cephalalgia* 2010;30:626-630.
32. Williams M, Bazina R, Tan L, Rice H, Broadley SA. Microvascular decompression of the trigeminal nerve in the treatment of SUNCT and SUNA. *J Neurol Neurosurg Psychiatry* 2010;81:992-996.
33. Bartsch T, Falk D, Knudsen K, Reese R, Raethjen J, Mehdorn HM, et al. Deep brain stimulation of the posterior hypothalamic area in intractable short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). *Cephalalgia* 2011;31:1405-1408.
34. Chaila E, Ali E, Rawluk D, Hutchinson M. 'Switching off' SUNCT by sudden head movement: a new symptom. *J Neurol* 2011;258:694-695.
35. Paliwal VK, Singh P, Kumar A, Rahi SK, Gupta RK. Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) with preserved refractory period: report of three cases. *J Headache Pain* 2012;13:167-169.
36. Favoni V, Grimaldi D, Pierangeli G, Cortelli P, Cevoli S. SUNCT/SUNA and neurovascular compression: new cases and critical literature review. *Cephalalgia* 2013;33:1337-1348.
37. Jin D, Lian YJ, Zhang HF. Secondary SUNCT syndrome caused by dorsolateral medullary infarction. *J Headache Pain* 2016;17:12.
38. Lambru G, Trimboli M, Tan SV, Al-Kaisy A. Medullary infarction causing coexistent SUNCT and trigeminal neuralgia. *Cephalalgia* 2017;37:486-490.
39. Kitahara I, Fukuda A, Imamura Y, Ikawa M, Yokochi T. Pathogenesis, surgical treatment, and cure for SUNCT syndrome. *World Neurosurg* 2015;84:1080-1083.
40. Williams MH, Broadley SA. SUNCT and SUNA: clinical features and medical treatment. *J Clin Neurosci* 2008;15:526-534.
41. Coskun O, Ucar M, Vuralli D, Yildirim F, Cetinkaya R, Akin Takmaz S, et al. MR tractography in short lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) patients: case reports. *Pain Med* 2017;18:1377-1381.
42. Ertsey C, Bozsik G, Afra J, Jelencsik I. A case of SUNCT syndrome with neurovascular compression. *Cephalalgia* 2000;20:325.
43. Maggioni F, Manara R, Mampreso E, Viaro F, Mainardi F, Zanchin G. Trigeminal neuralgia and trigeminal-autonomic cephalalgias: a continuum or simple co-existence? *Cephalalgia* 2010;30:752-756.
44. Putzki N, Nirkko A, Diener HC. Trigeminal autonomic cephalalgias: a case of post-traumatic SUNCT syndrome? *Cephalalgia* 2005;25:395-397.
45. Choi HJ, Choi SK, Lee SH, Lim YJ. Whiplash injury-induced atypical short-lasting unilateral neuralgiform headache with conjunctival injection and tearing syndrome treated by greater occipital nerve block. *Clin J Pain* 2012;28:342-343.
46. Hannerz J, Greitz D, Hansson P, Ericson K. SUNCT may be another manifestation of orbital venous vasculitis. *Headache* 1992;32:384-389.
47. Bichuetti DB, Yamaoka WY, Bastos JR, Carvalho Dde S. Bilateral SUNCT syndrome associated to chronic maxillary sinus disease. *Arq Neuropsiquiatr* 2006;64:504-506.
48. Eguia P, Garcia-Monco JC, Ruiz-Lavilla N, Diaz-Konrad V, Monton F. SUNCT and trigeminal neuralgia attributed to meningoencephalitis. *J Headache Pain* 2008;9:51-53.
49. Choi JY, Seo WK, Kim JH, Oh K, Yu SW. Symptomatic SUNCT syndrome associated with ipsilateral paranasal sinusitis. *Headache* 2008;48:1527-1530.
50. Ito Y, Yamamoto T, Ninomiya M, Mizoi Y, Itokawa K, Tamura N, et al. Secondary SUNCT syndrome caused by viral meningitis. *J Neurol* 2009;256:667-668.
51. Cascella C, Rosen JB, Robbins MS, Levin M. Resident and fellow section. teaching case: symptomatic SUNCT. *Headache* 2011;51:1022-1026.
52. Pong DL, Marom T, Pine HS. Short-lasting unilateral neuralgiform headache attacks with conjunctiva injection and tearing presenting as sphenoiditis. *Am J Otolaryngol* 2013;34:166-168.
53. Granato A, Belluzzo M, Fantini J, Zorzon M, Koscica N. SUNCT-like syndrome attributed to varicella-zoster virus meningoencephalitis. *Neurol Sci* 2015;36:807-808.
54. Mathew T, Srinivas M, Badachi S, Nadig R. Post herpes zoster SUNCT like syndrome: insights from two case reports. *Cephalalgia* 2018;38:399-401.
55. Kursun O, Arsava EM, Oguz KK, Tan E, Kansu T. SUNCT associated with Devic's syndrome. *Cephalalgia* 2006;26:221-224.
56. Vilisaar J, Constantinescu CS. SUNCT in multiple sclerosis. *Cephalalgia* 2006;26:891-893.
57. Bogorad I, Blum S, Green M. A case of MS presenting with SUNCT status. *Headache* 2010;50:141-143.
58. ter Berg JW, Goadsby PJ. Significance of atypical presentation of symptomatic SUNCT: a case report. *J Neurol Neurosurg Psychiatry* 2001;70:244-246.
59. Morís G, Ribacoba R, Solar DN, Vidal JA. SUNCT syndrome and seborrheic dermatitis associated with craneosynostosis. *Cephalalgia* 2001;21:157-159.
60. Sebastian S, Schweitzer D, Tan L, Broadley SA. Role of trigeminal microvascular decompression in the treatment of SUNCT and SUNA. *Curr Pain Headache Rep* 2013;17:332.
61. Zhang X. Trigeminohypothalamic tract. In: Gebhart GF, Schmidt RF, editors. *Encyclopedia of Pain.* 2nd ed. Berlin: Springer-Verlag Berlin Heidelberg, 2013;4082.
62. Kao YH, Hsu YC. Chiari malformation type I presenting as cluster-like headache. *Acta Neurol Taiwan* 2015;24:122-124.
63. Kim DE, Park JY, Ha H, Yoon GJ, Cho BH, Lee SH. Cluster-like headache secondary to focal cervical myelitis. *Neurologist* 2017;22:138-140.
64. Budhram A, Leung A, Sangle N, Khaw AV. Diffuse large B-cell lymphoma of the nasopharynx presenting with cluster-like headache. *Headache* 2017;57:806-808.
65. Kuritzky A. Cluster headache-like pain caused by an upper cervical meningioma. *Cephalalgia* 1984;4:185-186.