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...
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 systematically 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-IIIβ 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 mmH2O, 12 × 10^6/L and 0.4 g/kg per day) and corticosteroids for 50 days, his vomiting improved.

Paroxysmal left-hemicranial headache with ipsilateral lacrimation, conjunctival injection, rhinorrhea and flushing. The headache came in bursts and was localized to the left hemicranium and left neck. He had headache attacks during the night that woke him up from sleep. Each attack lasted 60–120 seconds for once per hour. 10/10 on Visual Analog Scale. Touching the affected area could trigger the headache. Carbamazepine, lamotrigine and uptake oxygen in local hospital, but had get no significant effects.

Optical coherence tomography demonstrated generalized thinning of the right retina. Visual evoked potential showed that binocular amplitude was decreased, while the right amplitude was more severely reduced. The intraocular pressure of the right eye and left eye were 22.5 mm Hg and 20.3 mm Hg, respectively.

His headache disappeared but vision decreased again in February. Serum AQP4-ab was positive.
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)\(^3\) 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,\(^34,45\) 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,\(^3,7,14,16,18\) of which four were macroadenoma\(^3,7,16,18\) and three were pituitary microadenoma.\(^1,11\) The other six cases.
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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-

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).
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 non-functioning 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 the cavernous sinus (two cases with neoplasm) 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

| Disease Type | 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<sup>7</sup> | 26 | M | 20–30 | 1–6 | Yes | R | Cavernous sinus and carotid artery | BCT |
| | 2<sup>10</sup> | 33 | M | 10 | 1–10 | Yes | L | Cavernous sinus | DA |
| | 3<sup>18</sup> | 35 | F | 60–120 | 40 | Yes | R | Cavernous carotid artery | LMT |
| | 4<sup>3</sup> | 27 | F | 15–30 | N/A | Yes | L | Cavernous sinus | LMT |
| Pituitary adenoma | 5<sup>13</sup> | 46 | M | 15–120 | 3–6 | Yes | L | Cavernous sinus | CAB |
| | 6<sup>12</sup> | 22 | F | <60 | 5–10 | Yes | L | No extension | CAB |
| | 7<sup>10</sup> | 26 | M | 60 | 2–8 | N/A | L | No extension | Surgery |
| | 8<sup>14</sup> | 18 | F | 30 | 5–10 | No | B | No extension | LMT |
| Pituitary microadenoma | 9<sup>3</sup> | 24 | F | 15–30 | 10–30 | Yes | L | No extension | Surgery |
| | 10<sup>5</sup> | 28 | M | 20–30 | 100–200 | N/A | R | No extension | Surgery |
| | 11<sup>11</sup> | 33 | M | 60–120 | 30 | N/A | L | No extension | Surgery |
| Leiomysarcoma | 12<sup>6</sup> | 45 | M | 60–120 | 10–15 | Yes | L | Cavernous sinus | N/A |
| Pilocytic astrocytoma | 13<sup>4</sup> | 11 | F | 30–60 | 20 | No | R | Pons–CPA | Surgery |
| Epidermoid tumor | 14<sup>11</sup> | 33 | M | 30–60 | 240 | Yes | L | Pons–CPA | Surgery |
| Cyst | 15<sup>5</sup> | 23 | F | 10–60 | 20–30 | Yes | R | Ocular region | Surgery |
| Pulmonary metastases | 16<sup>13</sup> | 69 | F | 60–120 | 50–70 | Yes | R | Ocular region | Radiotherapy |
| Meningioma | 17<sup>13</sup> | 81 | F | N/A | 60 | No | 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.
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 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<sup>10</sup> | 33 M 30 360           | No  | L pons–CPA–arteriovenous malformation | CBZ                |
|                          | 19<sup>10</sup> | 55 M 30 280–360       | Yes | R pons–CPA–vascular malformation    | CBZ, AMT           |
|                          | 20<sup>7</sup>  | 43 F 30–45 6–7        | Yes | R pons–PCC–SCA               | MVD                |
|                          | 21<sup>5</sup>  | 54 F 60–120 N/A       | Yes | L pons–PCC–SCA               | MVD                |
|                          | 22<sup>6</sup>  | 47 M 60 30–40         | Yes | R pons–PCC–SCA               | MVD                |
|                          | 23<sup>5</sup>  | 67 M 1–60 <720        | Yes | R pons–PCC–SCA               | DBS                |
|                          | 24<sup>4</sup>  | 45 F Seconds 20–60    | Yes | L pons–PCC–SCA               | MVD                |
|                          | 25<sup>6</sup>  | 44 M 30–60 >20        | Yes | R pons–PCC–SCA               | OXA, LMT           |
|                          | 26<sup>7</sup>  | 57 M 30–120 120–240   | N/A | L pons–PCC–SCA VL            | MVD                |
|                          | 27<sup>7</sup>  | 54 M 5–10 3–10        | Yes | L pons–PCC–SCA VL            | MVD                |
|                          | 28<sup>7</sup>,<sup>40</sup> | 65 F 60–180 30–200   | Yes | R pons–PCC–SCA VL           | MVD                |
|                          | 29<sup>5</sup>  | 65 M 60–120 30–200    | Yes | R pons–SCA                  | N/A                |
|                          | 30<sup>7</sup>,<sup>40</sup> | 43 M 30–120 20–30    | No  | L pons–AICA                | LMT, lignocaine    |
|                          | 31<sup>7</sup>,<sup>40</sup> | 46 F 3–10 90–120     | Yes | R pons–SCA                 | LMT, lignocaine    |
|                          | 32<sup>7</sup>  | 44 F 30–120 100–300   | Yes | N/A Pons–SCA                | N/A                |
|                          | 33<sup>7</sup>,<sup>40</sup> | 19 M 20–180 8–10     | Yes | L pons–SCA                 | LMT                |
|                          | 34<sup>5</sup>  | 60 M 20–30 20–50      | Yes | R pons–PCC–SCA VL           | OXA, LMT           |
|                          | 35<sup>7</sup>  | 55 M 10–90 25–30      | Yes | R pons–SCA VL               | LMT                |
|                          | 36<sup>6</sup>  | 64 M 10–30 5–30       | Yes | R B pons–SCA VL             | CBZ                |
|                          | 37<sup>6</sup>  | 46 M 30–60 1–6        | Yes | R pons–SCA VL               | CBZ, IM            |
|                          | 38<sup>6</sup>  | 50 F 2–180 >100       | Yes | R pons–SCA VL               | MVD                |
|                          | 39<sup>4</sup>  | 48 M 20–30 15–20      | Yes | L pons–AICA                | None               |
|                          | 40<sup>7</sup>  | 68 M 60–120 3–7       | N/A | L pons–BA VL               | GBP                |
|                          | 41<sup>26</sup> | 55 M 30 20–30         | No  | L pons–vertebrobasilar      | None               |
|                          | 42<sup>9</sup>  | 52 M 360 N/A          | Yes | R pons–PCC–VA              | MVD                |
|                          | 43<sup>9</sup>  | 65 M Seconds N/A      | N/A | R pons–PCC–SCA, AICA       | MVD                |
|                          | 44<sup>5</sup>  | 46 F 60–120 N/A       | Yes | R pons–PCC–SCA             | MVD                |
|                          | 45<sup>1</sup>  | 69 F 120–180 N/A      | Yes | R pons–PCC–SCA             | CBZ                |
|                          | 46<sup>5</sup>  | 43 F 30–45 6–7        | Yes | R pons–SCA                 | MVD                |
|                          | 47<sup>7</sup>  | 40 F <300 2–30        | Yes | R pons–SCA                 | LMT, GBP, amitriptyline |
| Cerebellar infarction    | 48<sup>7</sup>  | 63 M 20–180 8        | Yes | L pons–ischemic–penumbra of cerebellar N/A |
|                          | 49<sup>5</sup>  | 54 M 20 10            | No  | R dorsolateral medulla      | None               |
|                          | 50<sup>7</sup>  | 64 M 3–10 1–4         | No  | L dorsolateral medulla       | N/A                |
|                          | 51<sup>7</sup>  | 58 M 20 12–15         | Yes | R dorsolateral medulla       | CBZ, GBP           |
| Cavernous angioma        | 52<sup>7</sup>  | 60 M 60 15–23         | N/A | 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.
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 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 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 lacrimal 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 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          | 20                   | M   | 20–60              | 160                 | Yes     | R         | None                     | CBZ                      |
| Whiplash injury                              | 54          | 62                   | F   | 120–240            | 40–50               | Yes     | R         | None                     | GON blocks               |
| Sinusitis                                    | 55          | 53                   | M   | 5–10               | 144                 | Yes     | L>R       | B maxillary sinuses      | FESS                     |
| Ethmoid sinusitis                            | 56          | 71                   | M   | 3–5                | >100                | N/A     | R         | ocular region             | FESS                     |
| Sphenoiditis                                 | 57          | 62                   | F   | 60–240             | >20                 | N/A     | R         | sphenoid sinus            | AMX-clavulanate          |
| Orbital venous vasculitis                    | 58          | 49                   | M   | 300–600            | 1–180               | Yes     | R         | None*                    | Steroids, AZA            |
| Viral meningitis                             | 59          | 49                   | M   | 10                 | 100–200             | N/A     | R         | None†                    | Sumatriptan              |
| VZV meningoencephalitis                      | 60, 61     | 46, 72               | F, M| 30–60              | 240                 | No      | R         | None*                    | VPA                      |
| VZV                                          | 62, 63     | 58, 60               | M, M| 20                 | 96–120              | Yes     | R         | None                     | Pregabalin, LMT          |
| VZV                                          | 64          | 57                   | F   | 5–30               | 50–100              | No      | L         | Cervical spinal cord (C2/C3, C5/C6) | GBP                      |
| NMO                                          | 65          | 41                   | F   | 10–15              | 20                  | N/A     | L>R       | Medulla to cervical spinal cord (C6); ocular region | MP, IVIg                  |
| MS                                           | 66          | 18                   | M   | 5–30               | 20                  | N/A     | R         | R medulla; pons; cervical spinal cord. | N/A                      |
| Osteogenesis imperfecta                      | 67          | 59                   | F   | Seconds            | 720                 | N/A     | L         | L pons                   | Steroids, CMZ, IM        |
| Craniosynostosis brachycephaly               | 68          | 42                   | M   | 120–180            | 1–5                 | Yes     | L         | Basilar impression; L pons | CBZ                      |
| Craniosynostosis craniofacial                | 69          | 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.
The 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, infection, demyelination 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 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, Sebastian et al. and Favoni et al. 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

### 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 area | 2 (11.11) |
| Frontotemporal area | 1 (5.56) |
| Vascular disease (n=35) | |
| Pons | 32 (91.43) |
| Medulla | 3 (8.57) |
| Trauma (n=2) | |
| None | 3 (50) |
| 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) |
| Ocular region (n=1) | |
| Infection | 1 (100) |
| None (n=8) | |
| Infection | 6 (75) |
| Trauma | 2 (25) |
| No extension (n=6) | |
| Neoplasm | 6 (100) |
cases exhibited narrowing of the superior ophthalmic vein and a higher temperature around the ipsilateral orbital region. 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 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 that is associated with conjunctival injection or lacrimation. Chiari malformation type I, focal cervical myelitis, diffuse large-B-cell lymphoma of the nasopharynx, and upper cervical meningioma 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.

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