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MEDICINE

Secondary SUNCT Syndrome in a Patient with Rathke's Cleft Cyst and Hyperprolactinemia: a Case Report

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Abstract

Pathophysiology of short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) remains unclear. SUNCT is considered the primary type of a headache, but several cases of secondary SUNCT syndrome were described in patients with pituitary neoplasms, mainly pituitary micro- and macroadenomas. Rathke's cleft cyst is a suprasellar noncancerous cystic lesion. We described a new case of SUNCT in a patient with Rathke's cleft cyst with persistent hyperprolactinemia at the beginning of the headaches. After beginning of treatment with antiepileptic drugs (topiramate 75 mg/day, followed by replacement lamotrigine 75 mg/day), the headaches regressed. Also, cabergoline 0.5 mg was added to the therapy, 1 time a week; after 4 months, the level of prolactin was normalized, after beginning of dopamine agonists. After discontinuation of all treatments, after 4 months, the patient again began to develop daily single headaches, clinically similar to those that were at the onset of the disease, against the background of an increase in blood prolactin levels. Against the background of normalization of prolactin level, the headaches disappeared. We assume that in this case, the main reason for the secondary SUNCT was an influence of anatomical structures and caused neuroendocrine changes in the hypothalamus-pituitary system, but there are still discussions about what mechanism is the main reason for SUNCT. Therefore, clinicians should also pay attention to the history of symptoms associated with tumors in the pituitary gland and perform magnetic resonance imaging of the brain, pituitary gland, and screening for hormonal disorders in the blood serum.

Keywords SUNCT · Rathke's cleft cyst · Hyperprolactinemia · Trigeminal autonomic cephalalgia (TAC) · Case report

Introduction

Recurrent short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) were first described by Sjaastad et al. in 1978 as a separate and rare clinical disease [1]. According to the results of the studies, it is known that the average incidence is 1.2 cases per 100,000 inhabitants, and the prevalence is 6.6 cases per 100,000 inhabitants [2]. SUNCT is more often in men, the onset of the disease is mainly at the age of 40–50 years. The typical clinical picture is characterized by attacks of moderate or severe intensity; orbital, periorbital, or temporal localization; stabbing or pulsating pain lasting 5–250 s, with ipsilateral injection of conjunctiva; lacrimation; and rhinorrhea or nasal congestion. During the active periods, the frequency of attacks can range from 1 attack per day to more than 30 attacks per hour. Attacks are mostly daytime, and night attacks have rarely been reported [3]. Pathophysiology of this form of headache is still unknown, although studies using functional magnetic resonance imaging (fMRI) in spontaneous attacks have shown activation of the ipsilateral hypothalamic gray matter [4]. We described a new case of SUNCT in a patient with Rathke's cleft cyst and persistent hyperprolactinemia with a positive clinical response to topiramate and lamotrigine.

Although SUNCT is considered a primary type of headache, several cases of secondary SUNCT syndrome have been described, associated with affection of structures in the

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anterior and posterior cranial fossa, brain infarctions, meningitis, encephalitis, neuroinflammatory diseases, vascular abnormalities, and pituitary micro - and macroadenomas associated primarily with prolactinoma and acromegaly [5].

One of the possible types of masses in the anterior cranial fossa is Rathke's cleft cyst—a suprasellar non-tumor cystic mass that originates from the structures of Rathke's cleft cyst formed as a result of its incorrect involution [6]. Prevalence of these lesions is unclear, but they are now detected more and more frequently as imaging techniques improve and neuroimaging becomes more common. Symptomatic cases of Rathke's cleft cyst are relatively rare, and most of them are found accidentally. Etiology and pathogenesis of these lesions are not clear. Clinical manifestations of the Rathke's cleft cyst often appear when it begins to affect the surrounding structures. The most common symptoms include visual disturbances, headaches, and pituitary dysfunction (hypogonadism, hyperprolactinemia, hypothyroidism, growth hormone deficiency, hypocorticism, diabetes insipidus) [7, 8]. Treatment of symptomatic Rathke's cleft cyst is surgical resection, often through transsphenoidal access. However, up to 31% of cases of this pathology are characterized by a gradual decrease in the volume of the cyst at conservative treatment [9]. Therefore, due to the high risk of developing complications of the surgery, the choice of treatment is still open to negotiation.

Clinical Case

The patient, M. 33 years old, went to the headache treatment center a month after the onset of the disease with complaints of intense attacks of unilateral headache in the area of the brow, forehead, and behind the eye, accompanied by lacrimation on the pain side, conjunctival redness, rhinorrhea, and edema of the eyelid, lasting 60–120 s. During the attack, there was no nausea, vomiting, and light and sound phobia; the patient tried to stay in place, putting her hand to the place of pain to relieve the pain. The attacks were daily; at first they were single but gradually became more frequent up to 40–50 times a day, rarely at night. The patient could not determine the provoking factors. Painkillers, nonsteroid anti-inflammatory drugs (NSAIDs), and triptans did not result in a significant relief. Immediately after the onset of headache attacks, the patient visited a neurologist at the clinic and did an Indomethacin test—the result was negative and received treatment with carbamazepine 600 mg/d—without any effect. The patient was examined by an otolaryngologist, dentist, oculist, and maxillofacial surgeon, and no pathology was found.

There was no family history of such diseases. There were no abnormalities in the general somatic and neurological status.

In order to rule out the secondary SUNCT, the patient was referred to further examination. Magnetic resonance imaging (MRI) of the brain and pituitary gland with Gadovist contrast enhancement was performed and Rathke's cleft cyst (8 × 8 × 3 mm, 3 × 3 × 2 mm) was diagnosed. The patient was examined by a neurosurgeon, who did not find any indications for surgical treatment. In the hormonal status, the level of prolactin 2180 mIU/ml was significantly increased (norm 102–496 mIU/ml); other pituitary hormones were normal.

Treatment with topiramate was started with a gradual increase in the dose to 75 mg/day, at which the patient's headache attacks significantly decreased. Due to hyperprolactinemia, cabergoline 0.5 mg was added to the treatment—1/2 tab. Once a week, after 4 months the prolactin level normalized (375 mIU/ml), and the patient stopped taking it; there was no increase in headaches.

After few months of taking topiramate 75 mg/day, the headache attacks disappeared completely, but when she tried to reduce the dose or cancel the drug, they returned again. Topiramate was continued for up to 9 months with further replacement with lamotrigine 75 mg\day due to development of side effects (kidney microliths) for another 6 months.

After 4 months of discontinuation of lamotrigine treatment, the patient began to notice single daily headaches, clinically similar to those at the onset of the disease. A blood test for prolactin showed an increased level (546 mIU/ml). Against the background of resumption of cabergoline treatment, the prolactin level returned to normal (362 mIU/ml) within a month, and the headache also disappeared. Further observation of the patient for 3 months did not show any worsening of clinical symptoms.

Discussion

In order to determine primary or secondary nature of a headache, we follow the rule according to the international classification of headaches-3 (ICHD-3) [2]: when a new headache with the characteristics of trigeminal vegetative cephalalgia occurs for the first time in close temporal relation to another disorder that is known to cause headache or fulfills other criteria for causation by that disorder, the new headache is coded as a secondary headache attributed to the causative disorder.

In our patient, the new headache onset coincided with the identification of hyperprolactinemia in parallel with Rathke's cleft cyst. We assume that in this case, the main reason for the secondary SUNCT was an influence of anatomical structures and caused neuroendocrine changes in the hypothalamus-pituitary system, but there are still discussions about what mechanism is the main reason for SUNCT.

SUNCT pathogenesis is not yet clear, but it has been found that the posterior hypothalamus is involved in this process, which through an increase in production of orexins (including nociceptive orexin) activates the trigeminohypothalamic tract

and affects an activity of the trigeminal nerve nucleus. This leads to stimulation of the tregiminoparasympathetic system and activation of the pain pathway [10, 11].

Irritation of the trigeminal nerve triggers the trigeminal vegetative reflex, which is clinically manifested in a patient with a headache with vegetative symptoms. The activated trigeminal ganglion transmits excitation to the nuclei of the trigeminal nerve and the posterior horns of the spinal cord at C1 and C2 levels, from where second-order neurons transmit an impulse to the upper salivary nucleus in the brainstem bridge. Then preganglionic parasympathetic fibers depart from the upper salivary nucleus and go to the pterygoid ganglion, where postganglionic fibers depart from it, which eventually innervate the lacrimal gland and nasal and palate mucosa [12, 13].

In the cavernous sinus, the trigeminal, parasympathetic, and sympathetic nerve fibers are located close to each other, so invasion, dura mater stretching, or local pressure can affect the formation of secondary SUNCT [14].

As a rule, Rathke's cleft cysts that are asymptomatic have a diameter of less than 3 mm and are found in 13–22% of normal pituitary glands. Cysts with a diameter of more than 3 mm have more frequent symptomatic course [15]. Most often, Rathke's cleft cyst causes displacement of the anterior pituitary lobe in 40% of cases and of the posterior lobe in 20% of cases [16]. Along with the compression effects of the cyst, inflammation is believed to contribute to the destruction of the adjacent pituitary system and loss of pituitary function. The tendency for symptomatic lesions to appear in adulthood suggests a slow-growing mass that develops over time and remains subclinical until significant symptoms appear [17].

However, the dimensions of the Rathke's cleft cyst do not always result in a headache and pituitary dysfunction [18]. Although headache may be a purely subjective symptom, Fleseriu M. et al. showed in their studies that patients with even small dimensions of the Rathke's cleft cyst (maximum diameter is up to 10 mm) can experience severe non-pulsating headaches, mainly in the frontal parts; headache impact test-6 (HIT-6) scales up to 64 points, and after surgical decompression of the cyst, the headache decreased to 37 points of HIT-6 scale [19].

The case of our patient is also interesting because she had symptoms of hyperprolactinemia and was treated with dopamine agonists.

Dopamine is an important hypothalamic neuroendocrine inhibitor that affects the secretion of prolactin from the anterior pituitary. It is assumed that it plays an important role in the pathophysiology of primary headaches. In addition, in some of the described cases, a change in the headache phenotype was observed after administration of dopamine agonists, which suggests that headache syndromes may be a result of changes in the dopamine-prolactin axis, and not simply due to the mechanical effect of neoplasm, and it is possible that specific neuroendocrine pathways including the dopamine-prolactin axis are also able to activate SUNCT pathophysiology [20].

It has also been reported that dopamine agonists used to correct hyperprolactinemia cause SUNCT. However, in some cases, the administration of dopamine agonists did not affect the number of attacks and the initiation of attacks, as described in a number of articles, including our case [21]. Therefore, paradoxically, dopamine agonists can aggravate and alleviate SUNCT. The exact mechanisms of the effects of dopamine agonists on the dopamine-prolactin axis are yet to be known.

Conclusion

In our patient, the new headache onset coincided with the identification of hyperprolactinemia in parallel with Rathke's cleft cyst. Symptomatic Rathke's cleft cyst is a rare pathology with a wide range of clinical and neuroimaging features. Reactive inflammation and displacement of the pituitary anatomical structures can play a key role in the pathogenesis of hormonal disorders and contribute to the occurrence of SUNCT.

We assume that in this case, the main reason for the secondary SUNCT was an influence of anatomical structures and caused neuroendocrine changes in the hypothalamus-pituitary system, but there are still discussions about what mechanism is the main reason for SUNCT. Therefore, clinicians should also pay attention to the history of symptoms associated with tumors in the pituitary gland and perform magnetic resonance imaging of the brain and pituitary gland and screening for hormonal disorders in the blood serum.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethics Declarations The patient has consented to submission of this case report to the journal.

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