ORIGINAL ARTICLE

Intractable SUNCT Cured After Resection of a Pituitary Microadenoma

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ABSTRACT: ***Background:*** SUNCT is a rare primary headache disorder that is associated with activation of the posterior hypothalamus and often poorly responsive to medication. Recently, a relationship between between pituitary microadenoma and SUNCT has been suggested, and reports of both amelioration and exacerbation by dopamine-agonists have been published. These findings suggest a functional role for the hypothalamic-pituitary axis in SUNCT. ***Methods:*** We report the long-term 4 year follow-up of a 35 year-old patient with a 14-year history of medically and surgically intractable SUNCT who experienced immediate and complete resolution of symptoms after resection of a 6 mm pituitary microadenoma. ***Results:*** This patient was first seen at the age of 28 years with a 10-year history of attacks of right retro-orbital pain satisfying the IHS criteria for SUNCT. Many medical and surgical treatments were attempted without success. An MRI demonstrated a 6 mm microadenoma without compression of surrounding structures. A trial of bromocriptine caused marked exacerbation of his pain. The patient underwent a trans-sphenoidal resection of the pituitary lesion. SUNCT attacks worsened for the first 24h post-operatively, then disappeared. He has been completely headache-free, without medication, for the past 43 months with the last follow-up being January 2006. ***Conclusion:*** This case emphasizes the relationship between pituitary microadenomas and SUNCT, supports the role of the hypothalamic-pituitary axis in the genesis of SUNCT, and illustrates the importance of careful imaging of the pituitary region in patients with SUNCT.

RÉSUMÉ: Guérison d'un SUNCT réfractaire au traitement suite à la résection d'un microadénome pituitaire. ***Contexte :*** Le SUNCT (Short-lasting Unilateral Nevralgiform Headache with Conjunctival Injection and Tearing) est une forme rare de céphalée primaire qui est associée à une activation de l'hypothalamus postérieur et qui répond souvent mal à la médication. On présume maintenant qu'il existe une relation entre un microadénome pituitaire et le SUNCT. De plus, certaines publications font état d'une amélioration du SUNCT par les agonistes dopaminergiques alors que d'autres signalent une exacerbation. Ces données suggèrent que l'axe hypothalamo-pituitaire joue un rôle dans le SUNCT. ***Observation :*** Nous rapportons le cas d'un patient âgé de 35 ans qui a été suivi pendant 4 ans pour un SUNCT présent depuis 14 ans et résistant au traitement médical et chirurgical. Le patient a vu ses symptômes disparaître complètement immédiatement après la résection d'un microadénome pituitaire de 6mm. ***Résultats :*** Ce patient, qui se plaignait depuis 10 ans d'accès de douleur rétro-orbitaires droites satisfaisant aux critères de l'IHS (International Headache Society) pour le SUNCT, a été vu pour la première fois à l'âge de 28 ans. Plusieurs traitements médicaux et chirurgicaux ont été tentés mais sans succès. L'IRM a montré la présence d'un microadénome de 6mm sans compression des structures avoisinantes. Une tentative de traitement par la bromocriptine a exacerbé sa douleur. Le patient a subi une résection trans-sphénoïdale de la lésion pituitaire. Les accès de SUNCT ont été exacerbés pendant les 24 premières heures après la chirurgie puis ont disparu. Il n'a pas eu de céphalée depuis 43 mois, sans médication. La dernière visite de suivi date de janvier 2006. ***Conclusion :*** Ce cas souligne la relation entre les microadénomes pituitaires et le SUNCT illustrant le rôle de l'axe hypothalamo-pituitaire dans la genèse du SUNCT et l'importance d'une imagerie minutieuse de la région pituitaire chez les patients atteints de SUNCT.

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Short unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is a rare syndrome characterized by frequent and brief paroxysms of severe, unilateral pain in the first trigeminal branch distribution, accompanied by ipsilateral conjunctival injection and tearing. The role of the hypothalamus in SUNCT has been demonstrated by functional magnetic resonance image (MRI) studies that have shown either unilateral[1] or bilateral[2] activation of the hypothalamic posterior gray matter during attacks. A first case of successful hypothalamic deep-brain stimulation in SUNCT has been published.[3] The disorder has generally been considered difficult to treat, though several recent reports suggest that lamotrigine, lidocaine, gabapentin, and topiramate may be effective in selected cases.

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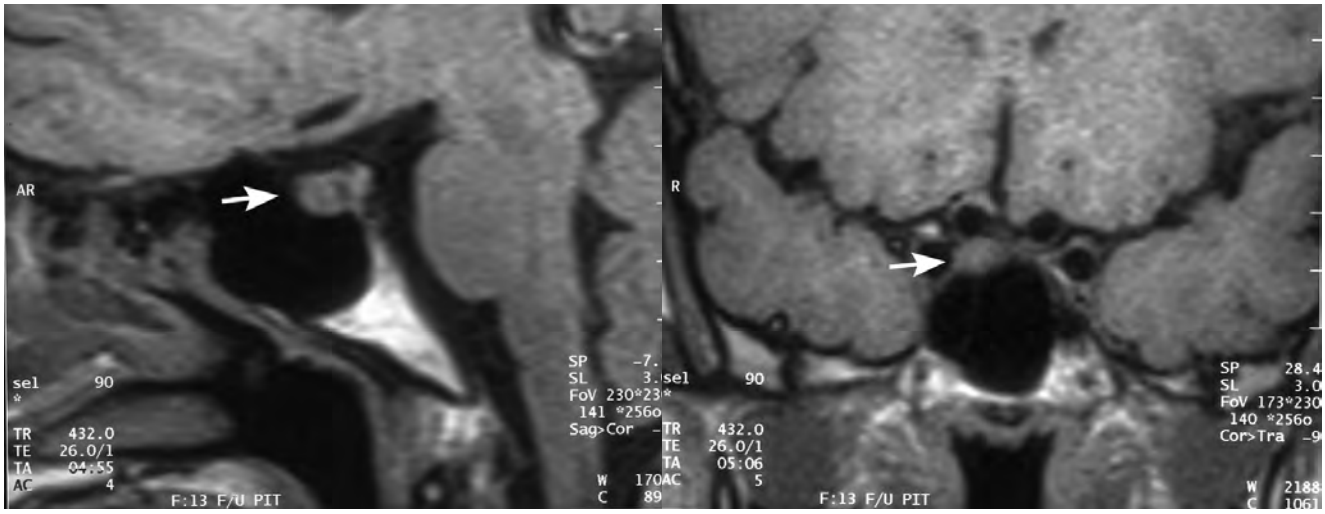

Figure 1 and 2. *MRI Brain: Sagittal and coronal T1-weighted images showing a 6 mm pituitary microadenoma (arrow) without suprasellar extension or compression of adjacent brain parenchyma.*

A number of patients with SUNCT have been reported with structural intracranial pathology. Treating the underlying lesion has been effective for cases of vascular trigeminal root compression, orbital cyst, intra-orbital carcinoid, pilocytic astrocytoma, and orbital venous vasculitis. In the absence of a lesion, glycerol rhizotomy of the trigeminal root and trigeminal root decompression have been successful in some patients, but without effect in others. Documenting the clinical response, whether positive or negative, of invasive treatments is important to provide appropriate care for these patients.

We report the four-year follow-up on a previously published[4] case of intractable SUNCT associated with a microproadenoma which was cured by trans-sphenoidal removal of the tumor.

Case Description

This patient was first seen in 1998 at the age of 28 years with a 10-year history of a sharp, piercing right retro-orbital pain that occurred 100-200 times a day, lasting 20-30 seconds. Attacks were accompanied by prominent ipsilateral tearing, rhinorrhea and conjunctival injection. The first MRI with and without contrast showed no lesion.

Many medical treatments were attempted without success, including indomethacin (75 mg TID), carbamazepine (800 mg per day), verapamil (240 mg sustained-release per day), lithium carbonate, verapamil (720 mg per day) divalproic acid, clonazepam, baclofen, gabapentin (3600 mg per day), lamotrigine (200 mg per day), topiramate (200 mg per day), clonidine, methysergide, ergotamine, dihydroergotamine and sumatriptan (6 mg subcutaneous). He underwent gamma knife radiosurgery (4 mm focus at a dose of 60Gy, isocenter at the trigeminal root exit zone) without any improvement after 12 months of follow-up. Five months later he had a microvascular decompression of cranial nerves five, seven, eight, nine and ten without benefit. Two months later, a microvascular decompression was repeated with section of the right nervus intermedius, with no relief, and sequelae of deafness, vertigo and disequilibrium from which the patient continues to suffer.

A subsequent MRI demonstrated a 6 mm microadenoma without suprasellar extension or compression of surrounding structures (Figure 1 and 2). The prolactin levels were high at 61.9 ng/ml and 54.3 ng/ml (normal value for men less than 23 ng/ml). Testosterone levels were low at 202 and 133 mg/dl (normal 241-827 mg/dl). He was treated with bromocriptine, and his attacks were markedly exacerbated. He required hospitalization for three days for pain control. A second trial of bromocriptine was initiated and again caused marked worsening of his symptoms requiring another hospital admission for several days. The patient was treated at that time with Oxycontin, 40 mg three times a day. He finally underwent a transsphenoidal hypophysectomy in June 2002 at another institution. Short unilateral neuralgiform headache with conjunctival injection and tearing attacks worsened for the first 24h post-operatively, then disappeared. Prolactin and testosterone levels normalized at 8.1 mg/ml and 668 mg/dl respectively. He has not had a single attack over the past 43 months.

Discussion

Although considered a primary headache disorder, a substantial proportion of published cases secondary to underlying structural pathology have been published. Associated lesions have been reported in the orbit, the cavernous sinus, near the trigeminal root in the ponto-cerebellar angle, in the brainstem, and with deformation of the posterior fossa. Lesion locations suggest mechanical or inflammatory stimulation of the trigeminal pathway with subsequent activation of the trigeminal-autonomic reflex.

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Association between pituitary tumors and SUNCT have somewhat challenged the compressive hypothesis in two ways. First, cases of SUNCT with non-compressive prolactinomas have been described.[5,6] Levy et al has demonstrated that size and invasion of the cavernous sinus were not significantly correlated with the presence of headache in 63 patients, implicating the potential for other mechanisms.[7] The association between different headache types and pituitary tumors has been recently reviewed, suggesting that cluster headache and SUNCT may be over-represented with these tumors.[8] Second, evidence of a role for hormonal factors in the pathophysiology of the attacks is accumulating. Cases of SUNCT modulation by dopamine-agonists strengthen this hypothesis, but both improvement[9] and reproducible worsening[5,6] have been described. Dopamine-agonist modulation of other TACs has been described.[5,10] More recently, clomiphene citrate has been used with success in a patient with SUNCT and low testosterone, but no documented pituitary lesion.[11] Our case supports a role for a non-mechanical effect of pituitary microadenoma in the genesis of SUNCT.

Conclusion

The genesis of SUNCT is complex. Functional imaging has demonstrated a clear role for the hypothalamus in patients with SUNCT. An MRI is recommended in all patients with SUNCT to exclude an underlying structural cause, given the range of structural intracranial pathologies that have been associated with this syndrome. The association between non-compressive functional pituitary microadenomas and SUNCT further emphasizes the role of the hypophyseal-pituitary axis in this disorder. This case confirms others in the literature and emphasizes the importance of the relationship between pituitary pathology and SUNCT. We believe that coronal MRI with special attention to the pituitary region and assessment of pituitary hormone levels are warranted in patients with SUNCT to exclude the presence of microadenoma, since targeted resection can be curative.

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