BLEPHAROSPASM INDUCED BY SYSTEMIC ISOTRETINOIN

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Abstract

Objective: Isotretinoin (13-cis-retinoic acid), a synthetic analog of vitamin A, is commonly used in the treatment of nodulocytic acne, which is resistant to other treatments. The most common side effects of systemic isotretinoin treatment are dry mucous membranes and dry skin. Blepharospasm is a movement disorder characterized by hyperactivity of orbicularis oculi and other muscles around the eye.

Case Report: We report here a 33-year-old female patient developed blepharospasm during treatment with systemic isotretinoin. She consulted an ophthalmologist about her eye problem and was diagnosed as having 'dry eye'. Blepharospasm did not improve even though she received artificial tears treatment. Magnetic resonance imaging and magnetic resonance angiography were performed to investigate the etiology of blepharospasm and no pathological findings were found.

Conclusion: We present a case of blepharospasm due to isotretinoin. Based on PubMed database, this is the first clinical case of blepharospasm induced by isotretinoin.

Keywords: Blepharospasm, isotretinoin, systemic

Introduction

Isotretinoin (13-cis-retinoic acid), a synthetic analog of vitamin A, is commonly used in the treatment of nodulocytic acne, which is resistant to other treatments (1). The most common side effects of systemic isotretinoin treatment are dry mucous membranes and dry skin. The most important side effect of this drug is teratogenicity (2). Ocular adverse effects of isotretinoin are mostly dose related and they include meibomian gland atrophy, blepharoconjunctivitis, corneal opacities, decreased dark adaptation, intolerance to contact lens, increased tear osmolarity, keratitis, ocular sicca, ocular disturbance and photophobia (3).

Blepharospasm is a movement disorder characterized by hyperactivity of orbicularis oculi and other muscles around the eye (4). Blepharospasm can be divided into three groups: primary, secondary, and drug-induced. Drug-induced blepharospasm is most usually associated with neuroleptics, dopaminergic agents, antihistamines, calcium channel blockers, and noradrenaline and serotonin reuptake inhibitors (5). We report here a case developed blepharospasm during treatment with systemic isotretinoin. To our knowledge, this has not been reported in literature.

Case Report

A-33-year-old female patient had severe nodulo-cystic acne on the face of five years duration. The patient was started systemic isotretinoin at 30 mg / day (0.5 mg/kg/d). There were no side effects except dryness in the first five months of the patient. Blepharospasm and irritation on the left eye started at 6 months of treatment. That was increasing with anxiety, fatigue, bright light exposure and reading during the day and the complaint was on the other eye. She consulted an ophthalmologist about her eye problem and was diagnosed as having 'dry eye'. Blepharospasm did not improve even though she received artificial tears treatment. She had no accompanying systemic disease and was not taking any other medication concurrently. General physical examination was unremarkable. Laboratory test results were within normal limits. The patient was evaluated by the neurologist for neurological disorders that may accompany it. On examination, she was noted to have involuntary spasm. There was no significant family history, previous neurological disorder, or any movement disorders (including Parkinsonism, dyskinesia, and akathisia) except for blepharospasm. Magnetic resonance imaging and magnetic resonance angiography were performed to investigate the etiology of blepharo-

spasm and no pathological findings were found (Figure 1,2). The patient was treated with gabapentin 300 mg 2 * 1/2 tablet. The complaints were partially regressed, but spasm continued at the same level as reading or focusing on anything. Informed consent form was obtained from the patient. As a result of all these evaluations, the patient was evaluated as drug-induced blepharospasm. Isotretinoin and gabapentin therapy was discontinued. Blinking decreased within two weeks after the discontinution of isotretinoin therapy and was completely regressed within 1 month. Three month after cessation, she was almost free from blepharospasm.

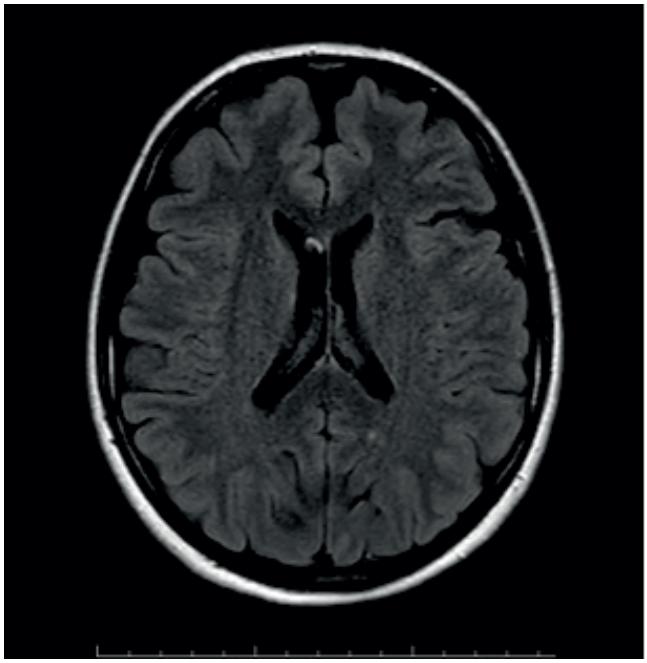

FIGURE 1. Normal serebral magnetic resonance imaging findings.

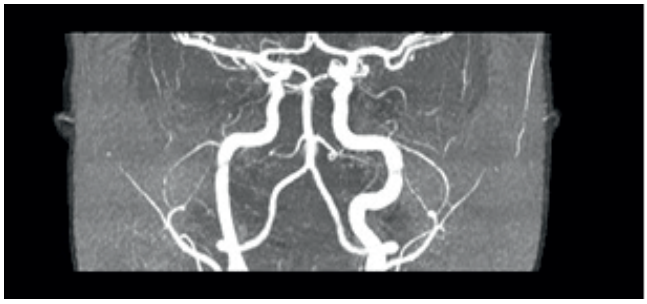

FIGURE 2. Normal serebral magnetic resonance angiography findings.

Discussion

Blepharospasm is characterized by stereotyped, bilateral and synchronous spasms of the orbicularis oculi muscles. The pathogenesis of blepharospasm is still not fully understood. The dysfunction of basal ganglia has traditionally been regarded as the main cause of many dystonic forms, but an increasing evident finding suggests that a network of additional cortical and subcortical structures may be involved (6). The primary form of blepharospasm is more common, and up to 25% of patients with blepharospasm have 1 or more family members affected by dystonia (4). Secondary blepharospasm is much less common than primary blepharospasm. Blepharospasm may follow focal lesions in multiple brain regions, including the thalamus, basal ganglia, lower brain stem, cerebellum, midbrain, and cortex or it accompanies other movement disorders such as Parkinson's disease (4,6).

Drug-induced blepharospasm may occur with antihistamines, dopaminomimetic, sympathomimetic drugs or prolonged exposure to dopamine antagonists (7). Although the pathogenesis of drug-induced blepharospasm is not clearly known, it is thought to be related to the abnormalities of the cortical or subcortical neural pathways (5). Drug-induced dystonia is divided into acute dystonia and tardive dystonia. Acute dystonia occurs after a one-time exposure to the drug. Symptoms may include intermittent spasmodic or non-continuous involuntary contractions on the face, neck, trunk and extremities, but the symptoms may be transient. Tardive dystonia caused by chronic exposure to dopamine antagonists (8).

Retinoids have immunomodulatory and anti-tumor properties, modify cell growth and differentiation, and assist in the treatment of acne by stimulating apoptosis of sebocytes. The most common side-effects of systemic isotretinoin treatment are dry mucous membranes, nose bleed, dry skin and eye dryness. Side effects of retinoids in the central nervous system are uncommon and vary from mild headache to vision changes and papillomedema (2). To the best of our knowledge, there has been no reported case of blepharospasm due to isotretinoin. The mechanism of blepharospasm formation in our case is attributed to ocular side effects of isotretinoin. Ocular side effects induced by isotretinoin use have been reported, resulting frequently from changes to the eyelids and the surface of the cornea or abnormal lacrimal gland

secretion that leads to dry eye (9).

Sensory signs reported by patients with blepharospasm include dry eye, grittiness in the eye and photophobia. Dry eye is common symptom, but objective measurements of tear production are usually normal. There may be some anomalies in the tear film itself or dryness sensation (4). Ophthalmological disorders may trigger idiopathic blepharospasm in predisposed patients. Eye symptoms may be part of the spectrum of blepharospasm but they can also result from eye diseases of the anterior segment of the eyes in blepharospasm patients (10). In our case, despite the application of artificial tear treatment due to dry eye, her complaints were not alleviated and partial response was obtained from gabapentin treatment.This suggests that pathways in the central nervous system may play a role in pathophysiology in isotretinoin-induced blepharospasm.

Despite the advances in etiopathogenesis, treatment of blepharospasm is still symptomatic. In treatment of blepharospasm, Botulinum neurotoxin type A is considered the first drug. Drugs such as anticholinergics (trihexyphenyl), benzodiazepines (eg, clonazepam and lorazepam), baclofen and tetrabenazine are widely used, but side effects can be problematic (4). In our case, gabapentin 300 mg 2 * 1/2 tablet was used and partial response was obtained. Discontinuation of isotretinoin treatment brought complete remission of the blepharospasm within 1 month. There was no recurrence in the patient who was followed for 3 months.

Conclusion

We present a case of blepharospasm due to isotretinoin. Based on PubMed database, this is the first clinical case of blepharospasm induced by isotretinoin.

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