ภาวะสีม่านตาสองข้างไม่เท่ากันในผู้ป่วยฮอร์เนอร์ที่เกิดภายหลัง ซึ่งเกิดจากการฉีกขาดของเส้นเลือดอินเทอร์นอลคาโรติด

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บทคัดย่อ

เพื่อรายงานเคสผู้ป่วยที่มีสีม่านตาสองข้างไม่เท่ากันในคนไข้กลุ่มอาการฮอร์เนอร์ชนิดไม่สมบูรณ์ที่เกิดขึ้นภายหลัง ซึ่งเกิดจากการฉีกขาดของเส้นเลือดอินเทอร์นอลคาโรติด ผู้ป่วยชายอายุ 23 ปี สังเกตว่าตนเองมีอาการหนังตาซ้ายตกเป็นเวลา 2 ปี แต่ไม่มีจุดเวลาชัดเจนของการเริ่มต้นเกิดอาการดังกล่าว จากการตรวจตาพบว่ารูม่านตาข้างขวามีขนาดใหญ่กว่าข้างซ้ายโดยจะเห็นชัดเจนในที่มืด (anisocoria) พบหนังตาซ้ายตก (ptosis) และพบว่าม่านตาข้างซ้ายสีอ่อนกว่าข้างขวา (heterochromia iridis) การกลอกตาปกติ การตรวจหาโรคไมแอสทิเนียเกรวิส (Myasthenia gravis) โดยใช้น้ำแข็ง (ice test) และตรวจการล้าของกล้ามเนื้อหนังตา (fatigability test) พบว่าผลออกมาปกติ คนไข้ปฏิเสธการตรวจบริเวณที่เหงื่อออกโดยใช้แป้งและไอโอดีน (starch iodine test) จากผลการตรวจทั้งหมดทำให้นึกถึงกลุ่มอาการฮอร์เนอร์แต่กำเนิด (congenital Horner syndrome) แต่อย่างไรก็ตามยังสามารถนึกถึงกลุ่มอาการฮอร์เนอร์ที่เกิดภายหลัง (acquired Horner syndrome) ได้ จึงทำการตรวจเพิ่มเติม ได้แก่ การตรวจสมอง เส้นเลือดสมอง และเส้นเลือดที่คอด้วยการตรวจเอ็กซเรย์คลื่นแม่เหล็กไฟฟ้า พบว่าเกิดจากการฉีกขาดของเส้นเลือดอินเทอร์นอลคาโรติดข้างซ้ายจนทำให้เกิดการตีบตันของเส้นเลือดดังกล่าว ซึ่งคาดว่าเป็นสาเหตุของกลุ่มอาการฮอร์เนอร์ ทั้งนี้เมื่อทำการตรวจหาสาเหตุเพิ่มเติมพบว่าคนไข้มีกลุ่มอาการเอเลอร์แดนลอส (Ehlers-Danlos syndromes)

คำสำคัญ: กลุ่มอาการฮอร์เนอร์ สีม่านตาไม่เท่ากัน การฉีกขาดของเส้นเลือดอินเทอร์นอลคาโรติด กลุ่มอาการเอเลอร์แดนลอส

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Heterochromia iridis in acquired Horner syndrome secondary to spontaneous internal carotid artery dissection

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Abstract

The aim of this study is to report a rare case of heterochromia iridis in Acquired incomplete Horner syndrome, secondary to spontaneous ipsilateral internal carotid artery dissection in patients with Ehlers-Danlos syndromes. A 23-year-old man complained of left-sided ptosis for two years, but the exact onset of ptosis was unconfirmed. At presentation, the pupils showed anisocoria, which was more apparent in the dark and mild left upper eyelid ptosis was detected. The slit lamp examination showed heterochromia iridis with iris hypopigmentation in the left eye compared to the right eye. The extraocular motilities were normal. The ice test and fatigability test were also negative. The starch iodine test for anhidrosis evaluation was denied by the patient. Left-sided Congenital Horner syndrome (HS) was suspected, but Acquired HS cannot be ruled out. The MRA of the brain include the neck and MRI vessel were done and severe stenosis along the entire course of left internal carotid artery (ICA) from left ICA dissection (ICAD) was shown to be a causal lesion of HS. After a thorough evaluation, the patient was found to have underlying and undiagnosed Ehlers-Danlos syndromes (EDS).

Keywords: Horner syndrome, Heterochromia iridis, internal carotid artery dissection, Ehlers-Danlos syndromes

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Introduction

Horner syndrome (HS) is a constellation of symptoms consisting of miosis, mild upper eyelid ptosis, and facial anhidrosis. HS results from an interruption of the sympathetic nerve supply to the eye[1] . If HS is congenital or the onset is before two years of age, heterochromia iridis with hypopigmentation on the affected side is typically found. But it is very rare in individuals with acquired HS[2] Incomplete HS, consisting of ptosis and miosis but no facial anhidrosis, is found in about 25% of patient with internal carotid artery dissection (ICAD)[3,4] ICAD classically presents with unilateral head, neck or face pain, focal cerebral ischemic symptoms, and HS.

The most common cause of spontaneous ICAD is idiopathic in which predisposing factors include family history of dissection, Ehlers-Danlos syndromes, Marfan syndrome, fibromuscular dysplasia and other connective tissue disease disorders. The authors report a case of acquired HS with heterochromia iridis caused by spontaneous ICAD in patient with Ehlers-Danlos syndromes[5-7].

Case report

A 23 year-old patient with no significant past medical history came to the ophthalmology department with a complaint of left-sided ptosis for 2 years. At presentation, Snellen visual acuities were 20/20 OD and 20/20 OS without correction. His extraocular motilities had full range of motion in both eyes. Confrontation visual fields were full-to-finger-count in both eyes. Neither enophthalmos nor exophthalmos was detected. Pupils were measured in light and dark conditions. In light, the pupils were measured 3 mm OD and 1.5 mm OS. In dark, anisocoria was more apparent with the pupils measuring 4 mm OD and 2 mm OS (Fig.1). Pupils were normally reacted to light both eyes. Relative afferent pupillary defects were not detected in both eyes. Adnexal examination showed mild upper eyelid ptosis OS. Interpalpebral fissure widths were measured 10 mm OD and 8 mm OS (Fig.2). Levator function was good. Ice test and fatigability test were negative. Cocaine test was not done as it is illegal in Thailand. Apraclonidine test was unavailable. The slit lamp biomicroscopy examination showed heterochromia iridis with iris hypopigmentation OS compared to OD. Intraocular pressure and fundus examination were entirely unremarkable. Patient denied doing starch iodine test for evaluation of anhidrosis but history of asymmetrical facial sweating was not reported.

Based on clinical presentations, left-sided Horner syndrome (HS) was diagnosed. But the onset of HS cannot be confirmed because no childhood photograph was shown whether ptosis and pupillary miosis was presented. Thus, acquired HS cannot be ruled out. The patient was referred to a neurologist. Imaging studies were done for further work up the etiology of HS. Plain film chest was unremarkable. MRI brain was normal. MRA of brain and neck showed severe stenosis along the entire course of left internal carotid artery (ICA) with collateral supply by branches of left

internal maxillary artery to cavernous segment of left ICA (Fig. 3). The patient underwent MRI vessel wall to further clarify the cause of severe left ICA stenosis, and the result revealed left ICA dissection with intraluminal thrombus (Fig. 4). CTA whole aorta was done for aneurysmal surveillance and the result was unremarkable.

The patient had no prior headache, orbital, temple, throat and neck pain. He has history of delivery using forceps, so birth trauma cannot be excluded. He denied any other history of trauma. His blood pressure was always in normal limit. Family history showed first degree relative hemorrhagic stroke at the age of 43. The differential diagnosis includes Ehlers-Danlos syndromes, Marfan's syndrome, fibromuscular dysplasia, cystic medial necrosis and atheroma.

Physical examinations showed joint hypermobility based on The Beighton scoring system (score 8/9). He had neither prior muscle/tendon rupture, easy bruising nor joint subluxation. Skin features and facial appearances were normal. No atrophic scar, translucent skin and skin hyperelasticity were detected.

The patient underwent a molecular genetic testing for evaluation of vascular Ehlers-Danlos syndromes (EDS type IV) by sequencing analysis of *COL3A1,* the result showed that heterozygous pathogenic variant was not identified and gene-targeted deletion/duplication analysis was unremarkable. Thus, vascular Ehlers-Danlos syndromes (EDS type IV) was excluded. To identify subtype of EDS, further genetic testing should be conducted.

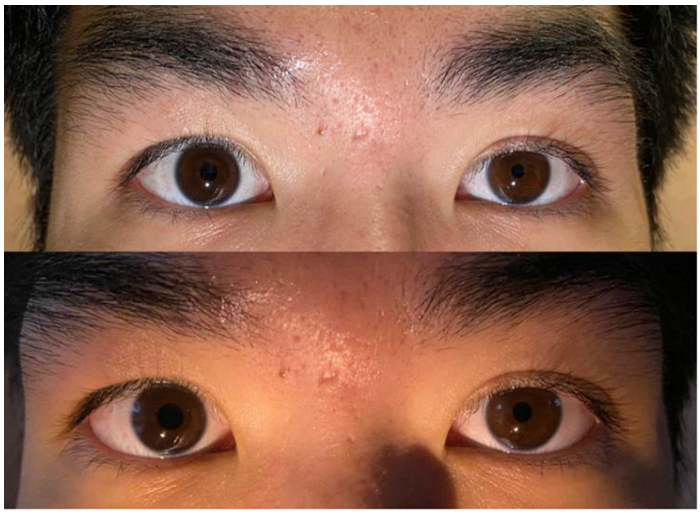

Figure 1 Anisocoria which is more apparent in dim light (lower picture) than bright light (upper picture)

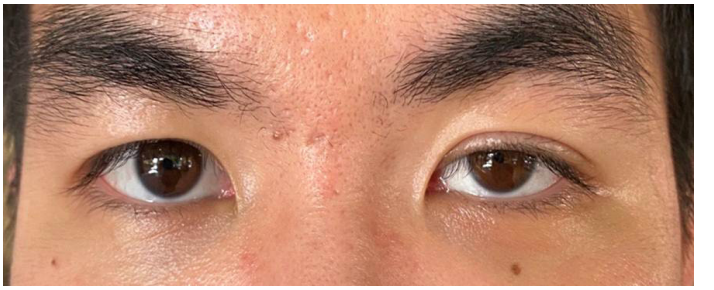

Figure 2 Mild upper eyelid ptosis OS with Interpalpebral fissure widths measured 10 mm OD and 8 mm OS and iris herterochromia which iris's color is lighter in left eye

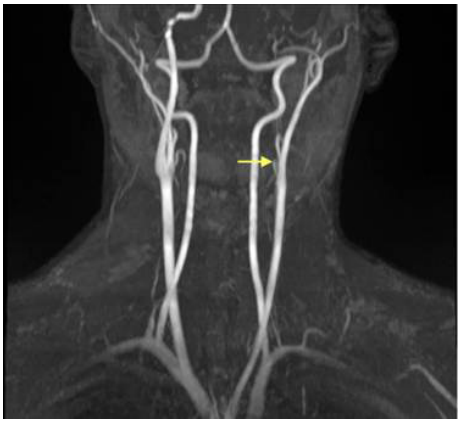

Figure 3 MRA of brain and neck showed severe stenosis along the entire course of left internal carotid artery (yellow arrow) with collateral supply by branches of left internal maxillary artery to cavernous segment of left ICA

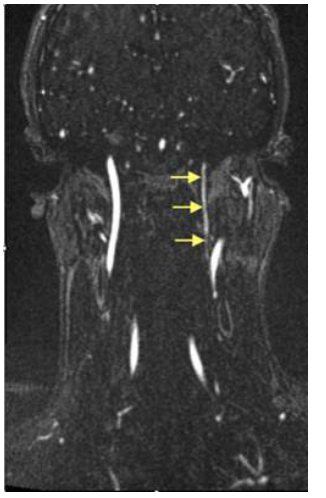

Figure 4 MRI vessel wall showed severe left ICA stenosis (yellow arrow), and revealed left ICA dissection with intraluminal thrombus

Discussion

Horner syndrome (HS), also known as oculosympathetic palsy, is a constellation of symptoms consisting of ipsilateral miosis, mild upper eyelid ptosis, and facial anhidrosis. HS is caused by interruption of at least one of the three neurons in the oculosympathetic pathway that originates in the hypothalamus. First-order neuron HS is caused by lesions of the sympathetic tracts in the hypothalamus, thalamus, brainstem or cervicothoracic spinal cord. Second-order neuron HS is caused by lesions involving the spinal cord, thoracic outlet, or lung apex. Third-order neuron HS is caused by lesions of the internal carotid artery, cavernous sinus[1].

Heterochromia iridis is characterized by color differences of the iris due to asymmetrical concentration and distribution of melanin in iris[8]. Heterochromia iridis is generally described in congenital HS or the onset of HS is before two years of age, but it can rarely be found in long-standing, acquired HS[2]. However it has never been found in patients with an acute or recently acquired HS. The mechanism of heterochromia iridis in congenital HS is about sympathetic influence on melanophore travelling into the iris and choroid in late gestation and early postnatal period. The trophic mechanism modulated by the sympathetic nervous system is retained within the eye. Thus, interruption of the sympathetic supply leads to failure of migration of this neural crest-derived melanocytes causing reduction in melanocytes in the anterior border and stromal layers. As a result, the iris remains hypopigmented[3,9,10]

Less commonly, heterochromia iridis in acquired Horner's syndrome has been reported but it is very rare. From literature review, there are only a few cases were reported to have an acquired HS with heterochromia iridis[11-13]. In all reported cases, the causal lesions were postganglionic in origin. Electron microscopic study identified contacts between melanocytes and nerve terminals in the stroma of the human iris. There are four distinct types of nerve terminals which at least two of these were adrenergic in origin. Thus, a disruption of the postganglionic pathway leads to a neurotropic dysgenesis of iris melanocytes. And adrenergic innervation is important in the maintenance of iris pigmentation[10]. These describes the present case of acquired Horner's syndrome with ipsilateral hypochromic iris.

In this case, the patient presented with HS with heterochromia iridis which usually described in congenital HS or early onset HS. The onset of HS could not be confirmed. Birth trauma cannot be excluded because of delivery using forceps. Additionally, no other obvious events was shown to be a cause of HS. So congenital HS was suspected. From literature review, heterochromia iridis can also be found in long standing acquired HS despite it is very rare. Furthermore, family history showed evidence of artery dissection in first degree relative. Thus, acquired HS cannot be ruled out. Further investigation to identify the

causal lesion of HS is necessary in all case suspected acquired HS. Imaging of brain, neck and vessel revealed severe stenosis of left ICA from left ICAD.

ICAD is a condition that results from the blood infiltration through a tear in the intimal layer and subsequently form intramural hematoma in vessel wall of ICA which cause ICA stenosis[5,6]. ICAD can be spontaneous or traumatic. In this case spontaneous ICAD was diagnosed due to no history of trauma.

The most common cause of spontaneous ICAD is idiopathic in which predisposing factors include family history of dissection and connective tissue disease disorders. Patient with ICAD classically presents with unilateral head, neck or face pain, focal cerebral ischemic symptoms, and HS. In individuals with ICDA, HS is the most common finding and in half of cases is the initial and sole manifestation like this presented case. Because its presentation is widely range from asymptomatic to one presenting with acute stroke, to make diagnosis on initial presentation is very difficult[7]. After a thorough evaluation, the patient was found to have underlying undiagnosed Ehlers-Danlos syndromes (EDS) which was thought to be a cause of ICAD.

Conclusion

Heterochromia iridis is generally described in congenital HS or the onset before two years of age, but it can rarely be found in long-standing, acquired HS. The present case shows heterochromia iridis in acquired HS resulted from spontaneous ICDA in patient with Ehlers-Danlos syndromes which has been rarely reported in the literature. This case indicates that full investigation to identify the causal lesion is warranted in a patient that acquired HS cannot be ruled out.

Acknowledgement

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