

The little old adie pupil

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Sri Lanka Journal of Neurology, 2013, **2**, 19-20

Introduction

The Holmes-Adie pupil (HAP) consists of tonic pupil/s of unknown aetiology. When HAP is associated with areflexia of lower limbs it is called Holmes-Adie's syndrome (HAS)¹. When HAS is associated with hypohidrosis it is called Ross Syndrome, although some consider it as a variant of HAS². When there is bilateral tonic pupil and areflexia it is important to differentiate whether the tonic pupils are due to HAS or peripheral neuropathy.

Case report

A 56-year-old previously healthy female presented with dull right sided headache without sinister features for three days. She was reviewed in the neurology clinic 2 weeks later. She had anisocoria with right pupil 4 mm in size and the left 6 mm. Both pupils reacted poorly to light and slowly reacted to accommodation (Figure 1A, B & C). In the left pupil sector palsy was noted and segmental vermiform movements were noted on slit lamp examination and local pathology in the iris and anterior chamber was excluded. Patient's eye movements were full and ophthalmoscopy revealed normal discs with

intact venous pulsations. Rest of the cranial nerve examination and the general neurological examination were normal except for absent ankle jerks. The patient did not have hypohidrosis or other autonomic manifestations.

Diluted (0.125%) pilocarpine constricted both pupils (Figure 1D). Fasting blood sugar, full blood count, blood picture, renal and liver function panel, thyroid function test, erythrocyte sedimentation rate, anti nuclear antibody test, magnetic resonance imaging of the brain with magnetic resonance angiogram and nerve conduction study of the lower limbs were all normal.

Discussion

Headache with dilated pupil is usually considered as a sinister sign. This patient did not have any other features to suggest a sinister headache. Her eye movements were full and there was no ptosis. Isolated pupillary abnormality as a manifestation of oculomotor nerve palsy is an extremely rare occurrence without diplopia, squints or ptosis³.

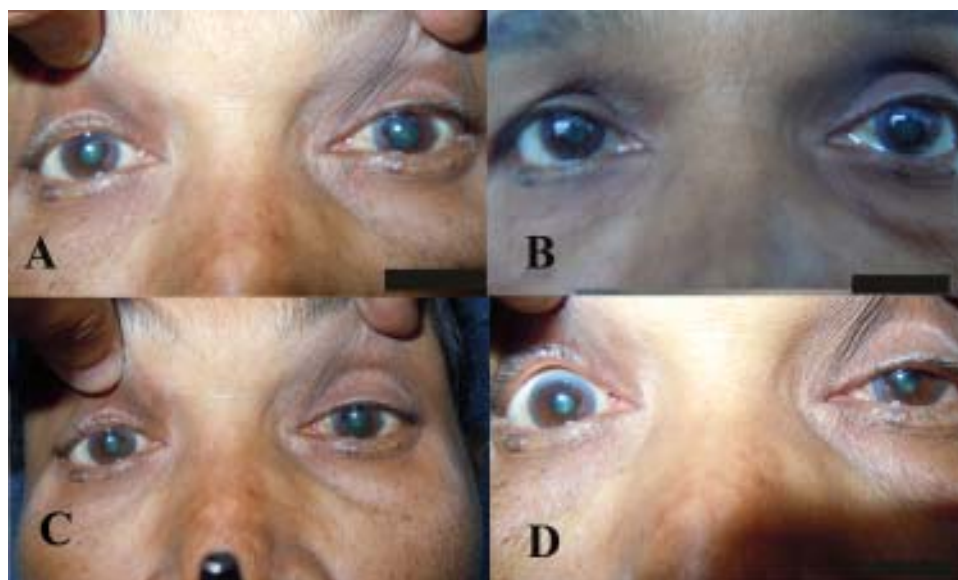


Figure 1. A: Pupils in light, B: Pupils in dim light, C: Pupils in accommodation, D: Pupils after diluted pilocarpine.

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When pupillary sizes differ more than 0.4 mm, it confirms anisocoria. To localize the abnormal pupil one can consider examination of the pupils in dim light which did not cause any change in size of the pupils in our patient (Fig 1B). Both pupils poorly reacted to light and slowly constricted to accommodation. There are a few causes to be considered in Light-Near dissociation (LND) syndromes such as Adie tonic pupil, Parinaud dorsal midbrain syndrome, Argyll Robertson pupils, oculomotor nerve aberrancy and peripheral neuropathy⁴. Argyll Robertson pupils are bilateral small pupils and are not keeping with this patient's findings. She did not have clinical features to suggest Parinaud syndrome or oculomotor nerve aberrancy. Segmental paralysis (sector palsy) of the iris sphincter with intact segments constricting to light with vermiform movements observed on slit lamp examination in the absence of structural iris damage confirms postganglionic oculo-parasympathetic lesion and excludes a third nerve palsy in our patient⁵.

Adie tonic pupil is caused by a lesion in the postganglionic parasympathetic pathway which is the ciliary ganglion or short ciliary nerves in the orbit. There are various aetiologies recognized such as trauma, tumour, ischemia, autoimmune, infection and idiopathic⁶. In the acute stage of the disease both iris sphincter and the ciliary muscle are paralyzed. The pupil does not react to light or accommodation initially. At this stage there may be photophobia, brow ache and blurring during near vision⁶.

As in many denervated end organs the iris sphincter also develops denervation supersensitivity usually in about one week. Diluted pilocarpine (0.125%) would constrict the denervated pupil but not the normal at this stage. A positive response is considered as either the effected pupil constricts 0.5 mm more than the normal pupil or the relatively larger abnormal pupil becomes the smaller pupil after the instillation⁶. In our patient both pupils constricted to pilocarpine and confirmed bilateral denervated hypersensitivity. Diluted pilocarpine test is neither specific nor particularly sensitive for Adie Pupil. This test also becomes positive in preganglionic denervation that is seen in oculomotor nerve palsy⁷. Cholinergic supersensitivity is absent in about 20% of tonic pupils⁶.

After the acute denervation, short ciliary nerve fibers tend to reinnervate to reach their end organs. During this process, resprouting accommodative fibers innervate the ciliary muscle and improve near vision. Relative abundance of accommodative fibers in comparison to pupilloconstrictor fibers results in aberrant reinnervation of the iris sphincter and restores the pupil near response in a few weeks. However the constriction movement and re-dilatation after a near effort is slow and it is called a tonic pupil. Because of the relative deficiency of pupilloconstrictor fibers, light reflex never improves. Due to the tonic firing of the accommodative fibers, baseline

size of the Adie pupil reduces with time and become the smaller pupil ("Little old Adie") which was seen in the right pupil of this patient.

With clinical features of bilateral absent ankle jerks, Holmes Adie Syndrome was considered in our patient. Although the nerve conduction test was normal small fiber neuropathy could not be excluded. When a patient present with unilateral tonic pupil and areflexia who is otherwise healthy the diagnosis of HAS is straightforward. However our patient had bilateral tonic pupils with areflexia which could be due to HAS or peripheral neuropathy in which it is utmost important to rule out the possibility of peripheral neuropathy causing the tonic pupils since HAS is a benign condition. A large European study (140 patients) with bilateral tonic pupils demonstrated that presence of sector palsy, anisocoria more than 1mm in light giving specificity (89.7%) to HAS and LND further increase the specificity to 92.3%. HAS affects one pupil first and may involve the fellow pupil often years later which makes anisocoria significant, where as the peripheral neuropathy affects both pupils together⁸. In HAS involvement of the fellow pupil is at a rate of 4% per year⁴. However bilateral tonic pupil at the initial presentation is rare and results in a diagnostic challenge. Presence of all these features in our patient led to a diagnosis of HAS. HAS remains a benign condition and patients do not progress to develop generalized neuropathy although the areflexia would be permanent⁸. Refractory correction and pilocarpine eye drops for the dilated eye can be considered to correct the near vision.

References

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