Diabetic patient with peripheral neuropathy and Holmes-Adie pupil

In the last of our case studies highlighting various presentation relating to diabetes, **Kirit Patel** describes a patient with diplopia and a second with a pupil anomaly

CASE ONE

Peripheral neuropathy

A 66-year-old diet-controlled diabetic visited the practice for his annual routine diabetic assessment. His main complaints were that his double vision in the distance appeared to have worsened over the past year. His current medication included Tamsulosin for prostate enlargement and diclofenac for pain.

History

In 1990 the patient developed peripheral neuropathy and a year later experienced his first bout of diplopia which he could control without need for prisms. By 1994, 1.5Δ base out controlled his esotropia. There was no motility defect and no signs of muscle palsy or ophthalmoplegia. The prism had increased to 4Δ base out in each eye by 1996. There was a gradual increase to 6Δ base out in each eye and he was referred in 2003 to an orthoptist via an ophthalmologist. The ophthalmologist agreed it was a decompensating esotropia. The patient was also under the care of the neurologist for peripheral neuropathy. Exercises were given by the orthoptist and prisms were incorporated in his spectacles. By 2005, the prism had increased to 7Δ base out in each eye and again this was incorporated in his distance prescription.

Findings this visit

Distance prescription

R +2.00DS = 10Δ Base out VA 6/6
L +2.25DS / -0.25DCX 20 = 10Δ base out VA 6/6
20Δ esotropia left eye.

Near prescription

R +4.00DS = 4Δ base out VA N5
L +4.25DS / -0.25DC X 20 = 4Δ base out VA N5.
8Δ esotropia left eye.

Hess screen plot (Figure 1)

- Hess screen plot revealed equal fields for both the right eye and the left eye indicating this was not an incomitant squint due to nerve palsy
- The centre indicated by red dot is displaced nasally as marked by the blue and this suggests an esotropia.

Decision taken

The patient was concerned about the double vision and was referred to another consultant with a view to whether surgery would be beneficial at this stage.

He was given a thorough examination by the consultant and an MRI scan to rule out any pathology of the brain stem or cerebral vascular cause. The scan showed no abnormalities for the diplopia. The patient was also booked to have surgery for his esotropia.

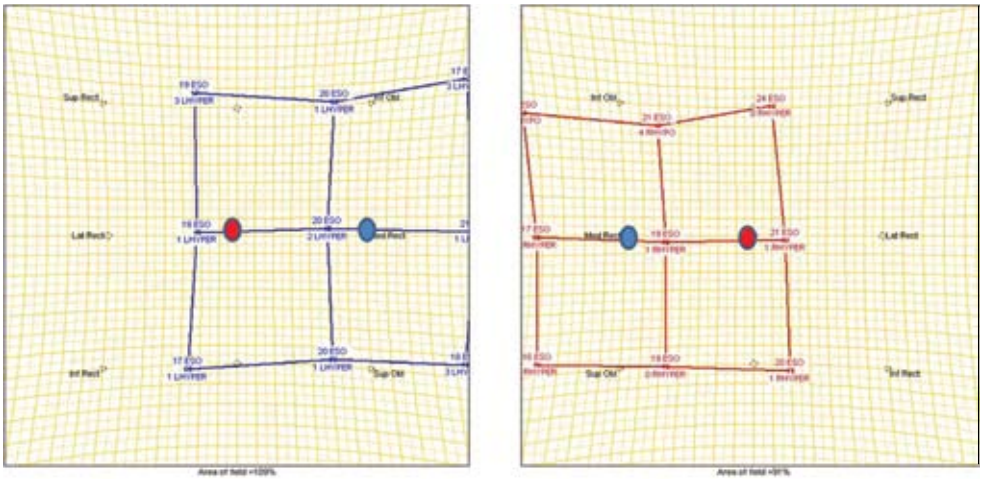


Figure 1 Hess screen plot

Conclusion

Remember, diabetic screening protocol does not take into account double vision and only a thorough eye examination would give a full assessment of the oculomotor system. The peripheral neuropathy was the red herring here and the cause of the diplopia was a decompensating concomitant esotropia.

Peripheral neuropathy is a term used to describe damage to the peripheral nerves and not the spinal cord and the brain. The nervous system consists of the central nervous system which is made up of the brain and spinal cord while the peripheral nervous system consists of nerves which carry messages between the brain, spinal cord and the rest of the body. The nerves that can be affected are motor, sensory or autonomic nerves and the symptoms experienced include numbness, sensitivity to touch, burning and tingling as well as muscle wasting or paralysis. Causes of peripheral neuropathy can be inherited or acquired. Acquired neuropathy could be physical damage to the nerve, vascular or nutritional metabolic disorders, tumours or autoimmune disease.

CASE 2

Holmes-Adie pupil

A 51-year-old female diet-controlled diabetic attended for an examination on the advice of her children who noticed that her right pupil appeared dilated. She had no real concerns except that she experienced some focusing difficulties. Six months previously she suffered a heart attack and in one swoop she had to take a selection of eight heart and blood medications along with asthma inhalers.

Spectacle prescription

R +0.75DS / -0.25 DC X 180 VA 6/6
Add +2.00DS N5
L +0.25DS VA 6/6 Add +2.00DS N5.

Ocular findings

- Right dilated pupil
- Right pupil reacts sluggish to direct and consensual light

- Right pupil remains dilated on convergence (Figure 2)
- Left pupil appears normal size
- Left pupil reacts normally to direct, consensual and near reflex (DCN)
- Intraocular pressures normal at R 18mmHg and L 16mmHg
- No diabetic retinopathy (R0).

Decision taken

The patient was told that she had a Holmes-Adie pupil and she was referred to a local consultant as a non-urgent referral. The referral letter consisted of the pupil images and the explanation that the right pupil appeared dilated under daylight and sluggish reaction to direct and consensual light. The other reason for referral was also to ensure that the left eye was not an Argyll-Robertson pupil resulting from tertiary syphilis.

By the time the patient saw the ophthalmologist the pupils had returned to normal. The pictures enclosed with the referral letter were solid proof and the consultant said how impressed he was with the quality of the referral letter and the images.

Pathopathology of Holmes-Adie pupil

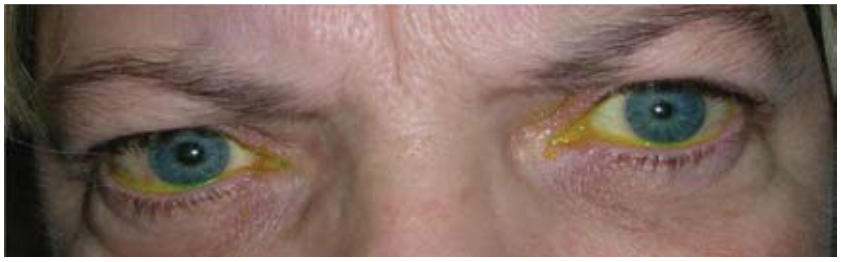
Holmes-Adie pupil is thought to be an inflammatory damage, secondary to bacterial or viral infection, to the autonomic ciliary ganglion leading to unilateral mydriasis. Young women are more at risk and patients complain of accommodative difficulties. Holmes-Adie syndrome also affects the tendon reflexes and patients may complain of excessive sweating. The affected pupil is dilated and slowly constricts in response to light. The mechanism for the Holmes-Adie pupil is thought to be lesion of the post-ganglionic parasympathetic pathway leading to denervation supersensitivity of the iris muscles. To gain a better understanding it is best to go back to the basics of the neuro-humoral transmission and the autonomic nervous system.

Autonomic nervous system and neuro-humoral transmission

The branches of the autonomic nervous system are the sympathetic and the parasympathetic system. The autonomic nervous system works as a 'push-pull' system whereby the dilating effect produced by the sympathetic nervous system is opposed by the miotic effect produced by stimulation of nerves in the parasympathetic system.

The autonomic nervous system works through neuro-humoral transmission which is propagation of nerve impulse

Figure 2 On convergence the right pupil remains dilated while the left constricts



In daylight the right pupil is dilated compared to the left pupil

across synapses and neuro muscular junctions by specific chemical agents (neurotransmitters) namely adrenaline and noradrenaline for sympathetic system and acetylcholine for parasympathetic system.

The parasympathetic nerve supply for both the iris sphincter and ciliary muscle originates in the third nerve nucleus and leaves the nucleus via the third nerve taking a long route and terminating in the ciliary ganglion. The post-ganglionic fibres leave the ganglion in short ciliary nerves at the back of the eye and pierce the sclera to innervate the sphincter and ciliary muscles.

At the axon action potential is propagated by influx of Na+ and efflux of K+. The arrival of the action potential at the nerve terminal facilitates an inward movement of calcium Ca++ leading to discharge of acetylcholine from storage vesicles into the synaptic cleft. The acetylcholine reacts with specialised receptor sites on the post junctional membrane and initiating a physiological response in the effector cell (Figure 3).

Partial parasympathetic denervation sensitises the iris to cholinergic drugs. Diluted 2.5 per cent methacholine or diluted low dose pilocarpine (0.125 per cent) produces miosis in the Holmes-Adie pupil while the unaffected eye will not constrict with the lower concentration of miotic.

● **Kirit Patel** practises in Radlett, Hertfordshire

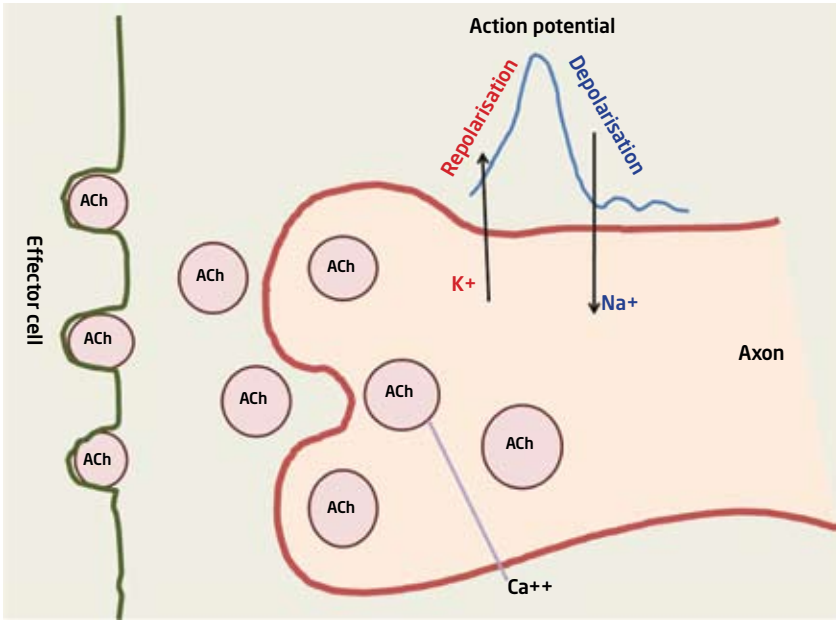


Figure 3 Neurotransmission of a synapse