Aberrant Regeneration of the Pupil: Lessons Learned

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Adie’s Pupil

- Acute denervation of postganglionic parasympathetic fibers to iris and ciliary body
- Almost always segmental palsy of iris sphincter
- Cholinergic supersensitivity within days
- After 8 weeks, aberrant regeneration of accommodative fibers to iris sphincter occurs, resulting in light-near dissociation
- Exuberant aberrant regeneration results in a small “little old Adie’s pupil in the chronic state.

Diagram of the Sympathetic and Parasympathetic Nerve Pathway to the Iris

Acute
- 6 weeks from onset
- Dark
- Bright Light
- Near
- Darkness
- 0.1% pilocarpine given to both eyes

Chronic
- 6 months later
- Dark
- Light
- Bright Light
- Near
- Darkness
- 0.1% pilocarpine given to both eyes

Adie Pupil - Segmental Sphincter Palsy
Slit Lamp Video

- Normal eye
- Equal sphincter contraction
- Abnormal eye
- Segmental sphincter palsy
Chronic “Little Old Adie’s Pupil”
Or “Tonic Pupil” Right Eye

- Dark
- Light
- Bright Light
- Near
- 0.5% tropicamide

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Segmental Denervation and Reinnervation of the Iris Sphincter as Shown by Infrared Videographic Transillumination

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Objectives: This study sought to evaluate the denervation and reinnervation history of individual segments of the iris sphincter in patients with Adie’s pupil.

Methods: In this study of 15 patients, the iris dilated was illuminated by using an infrared light through the lens itself. A video camera was directed toward the iris with an infrared sensitive video camera. The video images of each patient’s pupil were digitized through a video camera using infrared illumination. Images were recorded and stored on computer for analysis. The results were compared with histopathologic findings of the ipsilateral iris muscles.

Results: The iris dilated was illuminated by using an infrared light through the lens itself. A video camera was directed toward the iris with an infrared sensitive video camera. The video images of each patient’s pupil were digitized through a video camera using infrared illumination. Images were recorded and stored on computer for analysis. The results were compared with histopathologic findings of the ipsilateral iris muscles.

Conclusions: The correlation between the histopathologic findings and the video images of the iris dilated was demonstrated. The results of this study supported the hypothesis that the iris sphincter can be denervated and reinnervated by using infrared videographic transillumination.

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Why it is Important to Recognize Signs of Aberrant Regeneration:

- it indicates that the palsy is not acute
- it points to compression or trauma as cause
- it reveals that some recovery has occurred
- it explains unusual movements
- it may help formulate a surgical plan

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Injury (trauma or chronic compression)

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Disruption of Axons and Sheaths of Schwann

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Production of Neurotrophic Factors by Schwann Cells

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Axonal Sprouting

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Survival of Axons

Death of Axons

(re-innervation by misdirected nerve fibers) (no target effector found by axons)
Rules of Aberrant Regeneration

- Dennervation of the end organ is required
- Disruption of glial scaffolding within nerve bundles must occur

Re-innervation of a target muscle may be
- normal and complete
- incomplete or absent
- “aberrant” (wrong nerve to muscle)
- Re-innervation occurs from nerves with the same neurotransmitter as the original nerve

Primary Aberrant Regeneration
- Simultaneous paresis and Disordered regeneration
- No acute third nerve palsy

Compressive lesions:
- Tumor
- Aneurysm

Secondary Aberrant Regeneration
- Acute paresis followed By regeneration
- Does not occur following Ischemic third nerve palsy

Trauma is cause:
- head trauma
- neurosurgical trauma

Signs of Aberrant Regeneration

- Eyelid, ocular motility, and pupil signs of must be looked for independently or they will be missed!
- The abnormal movement should always be reproducible (“hard wiring” concept)
- Eyelid, ocular motility, and pupil signs may occur in isolation or in combination with each other
Oculomotor Aberrant Regeneration
Prevalence of End-Organ Involvement (50 cases)

Motility Signs of Aberrant Regeneration
May be subtle - lessening of an exotropia in upgaze or downgaze (best recognized using prism measurements)

Aberrant Regeneration of the Iris Sphincter Muscle
Important Considerations:
• Regeneration is proportional to loss of the light reflex
• Often segmental - slit lamp magnification may be needed
• Pupil may be the only sign (7/39 cases - 18%)
• Re-innervation of the iris sphincter may be from extraocular muscle nerves or accommodative nerves

Eyelid Signs of Aberrant Regeneration
Patient with left third nerve palsy

Examination of the Pupil in Oculomotor Nerve Aberrant Regeneration
An efferent pupil defect will be present
• The involved pupil will be the larger pupil in very bright light
• There may be no anisocoria in clinic light
• The involved pupil may be the smaller pupil in dim light (it fails to dilate normally)
Aberrant Regeneration of Iris Sphincter OD
“Reversing” Anisocoria from Light to Dark

Examination of the Pupil in Oculomotor Nerve Aberrant Regeneration
The pupil may not dilate in darkness:

- The iris sphincter is now innervated by nerves whose activity is not quieted in darkness
- The pupil dilates normally with anticholinergics
- The re-innervated pupil usually does not show cholinergic supersensitivity

Examination of the Pupil in Oculomotor Nerve Aberrant Regeneration
Change in anisocoria or pupil shape with change in gaze position
- The involved pupil constricts in one or more positions of gaze normally mediated by the oculomotor nerve (supraduction, infraduction, or adduction)
- Dilation occurs in the abducted position
- Small, segmental contractions of the iris sphincter with eye movement may be the only sign

Aberrant Regeneration of Iris Sphincter OD
By Misdirected Inferior Rectus Nerves OS
Left Pupil Contraction On Infraduction:

Aberrant Regeneration of Iris Sphincter OD
By Misdirected Medial Rectus Nerves OS
Left Pupil Contraction On Adduction:

Aberrant Regeneration of Iris Sphincter
By Misdirected Rectus Nerve Fibers OS
Segmental contraction of the iris sphincter with eye movements in a patient with misdirection dyskinesia

Pupil Pearls
Aberrant Regeneration

- Observe the pupils in bright light, clinic light, and dim light for anisocoria
- Put the normal iris sphincter innervation to rest by observing the pupils in dim light
- Constriction of the pupil in a gaze position should be reproducible for every observation
- Look for an abnormal near constriction of the pupil
- Segmental iris contraction on gaze or accommodation may be overlooked without slit lamp magnification

Pre-ganglionic sympathetic denervation of the iris dilator segmental palsy of some dilator sectors

Irregular Small Pupil After Neck Surgery for Tumor Removal

Pre-ganglionic sympathetic denervation of the iris dilator and aberrant re-innervation of some dilator sectors
Pre-ganglionic sympathetic denervation of the iris dilator and aberrant re-innervation of some dilator sectors

Sympathetics at superior cervical ganglion activated by swallowing!

Mystery Case – What is this?

Surprise Case – What is this?

An Additional Case

Oculomotor Nerve Palsy With Cyclic Spasms