Aberrant Regeneration of the Third Nerve

H C Chua, C B Tan, H Tjia

ABSTRACT

We describe three patients with aberrant regeneration of the third nerve secondary to traumatic brain injury. The full blown features of the syndrome include horizontal gaze-eyelid synkinesis, pseudo-Graefe sign, limitation of elevation and depression of the eye with retraction of the globe on attempted vertical movements, adduction of the involved eye on attempted elevation or depression, pseudo-Argyll Robertson pupil and absent vertical optokinetic response. The 'misdirection' incidence in our study is 15%.

Keywords: aberrant regeneration, third nerve, trauma, pseudo-Argyll Robertson

Singapore Med J 2000 Vol 41(9):458-459

INTRODUCTION

Aberrant regeneration of the third nerve is most commonly due to third nerve damage by trauma or aneurysm of the posterior communicating artery[1]. The full blown features include horizontal gaze-eyelid synkinesis, pseudo-Graefe sign, limitation of elevation and depression of the eye with retraction of the globe on attempted vertical movements, adduction of the involved eye on attempted elevation or depression, pseudo-Argyll Robertson pupil and absent vertical optokinetic response[2-5].

Over a one-year period from Nov 95 to Nov 96, we saw three patients with aberrant regeneration in our department. All cases were due to traumatic brain injury. During this time there were 20 patients with newly diagnosed third nerve palsies, giving a misdirection 'incidence' of 15%.

CASE REPORTS

Case 1

A 45-year-old Indian female jumped from a height of 4 storeys and sustained multiple injuries including brain contusion with a left third nerve palsy. Since then she complained of diplopia on right gaze. She defaulted follow-up and only consulted a doctor four years later when she complained of deteriorating vision after she started work as a computer programmer. Clinically, she had all the signs of aberrant regeneration of the third nerve (fig. 1).

Case 2

A 20-year-old Malay male with cerebral palsy and childhood seizures was referred by a general practitioner for poor seizure control. He had generalized tonic-clonic seizures about once a week and was non-compliant to medication. The patient's mother gave a history of a fall with head injury after he saw a snake twelve years ago. Subsequently she noted that he had a squint, but did not seek medical advice. Clinically he had a left third nerve palsy with aberrant regeneration. All signs were present except for pseudo-Argyll Robertson pupil. CT scan head was normal. He was treated with phenytoin but defaulted subsequent follow-up.

Case 3

A 40-year-old Chinese male was involved in a road traffic accident sixteen years ago. He sustained closed head injury with a right third nerve palsy. Since then, he complained of diplopia on both up and down gaze. However he was able to continue working as a grocery shop assistant. He was referred to the neurologist by his general practitioner for an unrelated complaint (carpal tunnel syndrome) and found to have aberrant regeneration of the third nerve.

DISCUSSION

Aberrant regeneration of the third nerve was first described by Gowers in 1879[6]. Bielschowsky in 1935 postulated that this condition was caused by misdirected regenerating third nerve fibres[7]. His hypothesis was supported by Bender and co-workers who produced aberrant regeneration in monkeys and abolished the paresis of upgaze by sectioning the inferior rectus muscle[8,9]. Co-contraction of extraocular muscles innervated by the oculomotor nerve with aberrant regeneration had been documented by ocular electromyography[10]. The concept of 'misdirection' was challenged by Lepore and Glaser who proposed two alternative mechanisms: ephaptic transmission (cross talk between axons) and central synaptic re-organization[11]. Ephaptic transmission occurs either centrally or peripherally at the site of nerve injury. Central re-organization occurs as a consequence of axonal

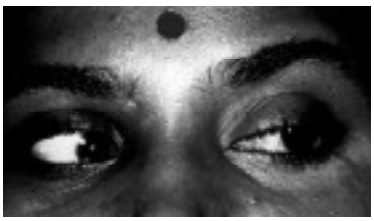
Department of Neurology
National Neuroscience Institute
1, Jalan Tan Tock Seng
Singapore 308433

H C Chua, MBBS, MRCP (UK), FAMS
Consultant

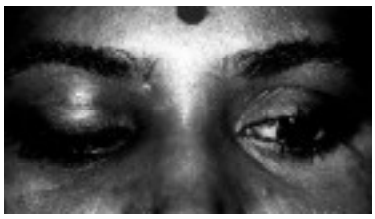
C B Tan, MBBS, MMED (INT MED), FAMS
Senior Consultant

H Tjia, MBBS, MMED (INT MED), FAMS
Senior Consultant and Head

Correspondence to:
Dr Chua Hoe Chin
Tel: 357 7171
Fax: 357 7137
E-mail: hoe_chin_chua@notes.ttsh.gov.sg


Look left


Look up and out on the left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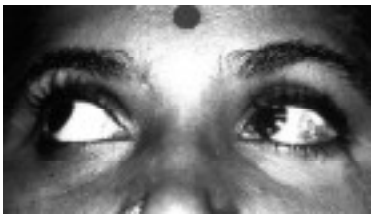
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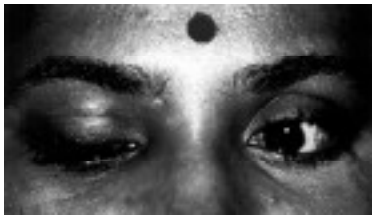
Look down and out on the right


Look straight ahead


Look up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injury inducing chromatolysis in the nerve cell body spreading to its central connections. This leads to oculomotor subnuclei reorganization resulting in aberrant regeneration.

In this study, third nerve palsy resulting in 'misdirection' was due to traumatic head injury in all cases[1,3]. Unfortunately we could not ascertain when synkinesis occurred as none of the patients were followed up serially. Another common cause is aneurysm of the posterior communicating artery. Less common causes include inflammatory conditions like cavernous sinus thrombosis, encephalitis-meningitis, syphilis, cholesteatoma of the temporal lobe, migraine, congenital third nerve palsies and a variety of primary and secondary brain tumors[2-5]. Primary progressive oculomotor misdirection is characteristic of intracavernous meningioma[12].

The full blown signs of aberrant regeneration of the third nerve include: (a) horizontal gaze-eyelid synkinesis-elevation of the involved eyelid on adduction of the eye; (b) pseudo-Graefe sign-retraction and elevation of the eyelid on downgaze; (c) limitation of elevation and depression of the eye with occasional retraction of the globe on attempted vertical movements; (d) adduction of the involved eye on attempted elevation or depression; (e) pseudo-Argyll Robertson pupil - although pupillary constriction may occur in any direction of gaze requiring third nerve function, it is seen most often with adduction. This resembles Argyll Robertson pupil since it is nonreactive to light but constricts with convergence. These changes are due to re-innervation of the postganglionic fibers serving sphincter function by collaterals from adjacent fibers not originally innervating the sphincter. Pseudo-Argyll Robertson pupil was seen in two out of three patients in our study; (f) absent vertical optokinetic response.

CONCLUSION

Aberrant regeneration of the third nerve may occur after third nerve damage from traumatic head injury. The full blown features of this syndrome may or may not be present.

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