Arq Neuropsiquiatr 2007;65(4-A):1007-1009

BILATERAL PTOSIS AND SUPRANUCLEAR DOWNGAZE PARALYSIS

Péricles Maranhão-Filho[1,2], João Carlos S. Campos[1], Marco A. Lima[1]

ABSTRACT - The purpose of this article is to highlight an uncommon combination of supranuclear downward gaze paralysis with bilateral eyelid ptosis in a 53-years-old man with a radiation induced midbrain tumor and to discuss the aspects regarding the centers and pathways that mediate supranuclear vertical gaze movements.

KEY WORDS: midbrain, rostral intersticial medial longitudinal fasciculus nucleus, downgaze paralysis, eyelid ptosis, tumor.

Ptose bilateral e paralisia supranuclear do olhar conjugado para baixo

RESUMO - O objetivo deste artigo é ressaltar uma rara condição caracterizada por paralisia supranuclear do olhar conjugado para baixo associada a ptose palpebral bilateral em um homem de 53 anos, causada por tumor mesencefálico radio-induzido, e discutir os aspectos relacionados ao controle supranuclear dos movimentos oculares verticais.

PALAVRAS-CHAVE: mesencéfalo, núcleo rostral intersticial do fascículo longitudinal medial, paralisia da mirada conjugada para baixo, ptose palpebral, tumor.

The structures and pathways that control the vertical eye movements are complex. In 1883, Henri Parinaud described three types of vertical gaze paralysis[1], which are: upgaze (most frequent); both upward and downward gaze simultaneously; and downgaze (uncommon). All three types may also be associated with convergence paralysis[2] and lid retraction[3]. Downgaze paralysis caused by a tumor has been rarely reported in the literature[1,4-6].

We describe a patient with bilateral eyelid ptosis, downgaze voluntary saccades, and pursuit paralysis due to a radiation induced midbrain tumor. We also discuss the aspects regarding the nuclei and pathways that mediate supranuclear vertical gaze movements.

CASE

A 53-year-old man underwent resection of a left cerebellar hemangioma and ventriculoperiteal shunting with adjuvant local field radiation therapy when he was fourteen years old. In May 2003, he started complaining of diplopia and developed ptosis on the left eye, which progressed in a few months to a bilateral ptosis. The symptoms and signs were not affected by eye movements, and did not fluctuate over the day. His general examination was unremarkable. By forcible frontal muscle contraction, we could observe a discrete left exotropia in primary eye position. He was not able to make downward saccades spontaneously or on command, and could not follow downward moving objects with smooth-pursuit eye movements. Upward and horizontal saccades and pursuit movements (Fig 1), as well as the horizontal and vertical doll's head maneuvers were intact. The *orbicularis oculi* strength was normal. Convergence was absent. Pupils were reactive to the light and symmetric. No other abnormalities were observed in the neurological examination.

The magnetic resonance imaging (MRI) (Fig 2) showed a midbrain lesion. A stereotaxic biopsy of this lesion revealed an anaplasic astrocytoma (WHO grade III).

Despite the treatment, the patient's neurological condition worsened, and he died 25 months after diagnosis.

Her sister gives us the written consent for this publication.

DISCUSSION

The midbrain houses centers and pathways that mediate supranuclear vertical gaze generation, neural integration in the vertical plane, and vergence movements. In this region, there are three key structures that control the vertical gaze[7]: a minute group of medium-sized cells located medial and dorsal to the rostral part of the red nucleus and lying interstitially within the medial longitudinal fasciculus (riMLF); the posterior commissure; and the interstitial nucleus of Cajal[1,6,7].

[1]Department of Neurosurgery, Brazilian National Cancer Institute, Rio de Janeiro RJ, Brazil; [2]Department of Neurology, Federal University of Rio de Janeiro, Rio de Janeiro RJ, Brazil.

Received 9 March 2007, received in final form 31 May 2007. Accepted 1 August 2007.

Dr. Péricles Maranhão-Filho - Avenida Canal de Marapendi 1680 / 1802 - 22631-050 Rio de Janeiro RJ - Brasil. E-mail: pmaranhaofilho @gmail.com

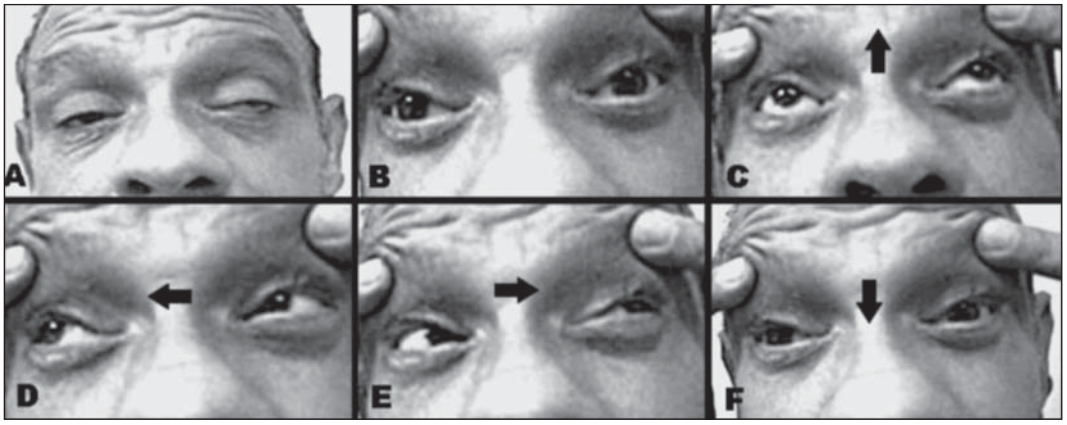

Fig 1. Eye movements (images taken from video). Bilateral ptosis with compensatory contraction of the frontal muscle and slightly left exotrophy in inert looking (A). Eyelid forcibly opened and symmetric pupils (B). Upward, right, and left eye movements (arrows indicate direction) are not limited (C,D,E). There was no movement down upon command (F) (or saccadic – not show).

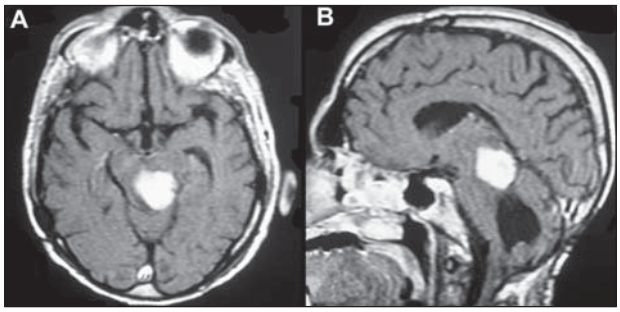

Fig 2. MRI T1-weighted sequence showing a contrast enhancing lesion in the midbrain tectum and tegmentum (A). In the sagittal view, the same enhancing lesion above a hypointense image in the cerebellum correspond the local area of the hemangioma resection and submitted a radiation thirty-eight years ago (B).

Taking into account both the clinicopathological findings and the results of experimental studies[1,3] we have a clearer impression that slightly different lesions in these three structures are responsible for central up versus downgaze paralysis[1,3,7]. The riMLF is the principal pre-motor structure for the generation of voluntary saccades in both vertical directions. Circumscribed and symmetric lesions in his efferent way result in downgaze paralysis[1,4,8]. The pre-motor areas controlling smooth pursuit movements are less clear[3].

The riMLF receives afferent innervation from regions controlling eye movements, such as the paramedian pontine reticular formation and vestibular nuclei, and sends efferent bilaterally to the oculomotor nuclei[1].

There is a separation between the burst neurons in the riMLF for pathways of upgaze and downgaze movements[2,3]. Upgaze prenuclear neurons send bilateral projections to the elevator muscles crossing within the oculomotor nuclear complex. In contrast, axons that mediate downgaze project ipsilaterally to the depressor muscles[2,8]. In our patient, although there was no pathologic study, we can conjecture an involvement of this second riMLF efferent axons by the tumor.

Another aspect to be considered is the bilateral ptosis presented by this patient. Eyelid movements are intimately coordinated with vertical eye movements[3,9]. Neural coordination of vertical gaze and lid position is due to a synkinesis between the vertical acting extraocular muscles and the *levator palpebrae* muscle[7]. There are some situations associating brainstem lesions and bilateral ptosis. Lesions to pathways coursing in the floor of the third ventricle and in the rostral midbrain, or in the central caudal nucleus (CCN), that is the small subgroup of the oculomotor nucleus containing levator motor neurons, may cause bilateral ptosis[3]. Destruction of the periaqueductally gray matter (PAG), can also lead to ptosis[9]. More rarely, bilateral ptosis associated with ophthalmoplegia may occur by an isolated lesion of an unilateral nuclear oculomotor complex[10]. Although there have been several indications that some central structures may be involved, the precise mechanism and pathways responsible by central bilateral ptosis until now remain unclear[3].

In respect to the tumor, even without knowing the first radiation therapy schedule and dosage, we can speculate that the anaplastic glioma was radiation induced. Radiation therapy has important late effects on the CNS. Prominent among these effects are the radiation necrosis of nervous tissue[11,12] and the appearance of tumors, which may be present as benign[13,14] or malignant[15,16]. Most of these are dose-

dependent and occur within the original radiation treatment field. They are usually meningiomas[17], sarcomas[18], or gliomas[19], but all types of nervous system neoplasms can occur[20,21]. Children receiving prophylactic irradiation for acute lymphatic leukemia have 22 times higher chance of developing CNS WHO grade II, III, and IV astrocytomas in the first five to 10 years after radiation therapy[19,20].

Similar to the Parinaud's syndrome[1], our patient presented with a vertical deficit of voluntary saccades and pursuit movements with preservation of oculocephalic reflexes. These aspects represent the fingerprint of the supranuclear nature of the process. However, our patient developed bilateral ptosis (no eyelid retraction) associated with downgaze paralysis (not up gaze paralysis). The convergence was impaired and pupillary reaction remained normal, which may or not occur in Parinaud's syndrome.

In conclusion, in light of the current knowledge and based on the neuro-ophthalmologic clinical examination and imaging aspects, we can assume the possibility of the involvement of the efferent riMLF connections and the central caudal nucleus, or the PAG, in a patient with midbrain radiation induced tumor.

Acknowledgement – The authors are in debit with Professor U. Buetnner for his critical review and manuscript suggestions and Péricles Maranhão Neto for his technical assistance.

REFERENCES

1. Pierrot-Deseiligny CH, Chain F, Gray F, Serdaru M, Escourolle R. Lhermitte F. Parinaud syndrome: electro-oculographic and anatomical analyses of six vascular cases with deductions about vertical gaze organization in the premotor structures. Brain 1982;105: 667-696.
2. Pearce JMS. Parinaud's syndrome: historical note. J Neurol Neurosurg Psychiatry 2005;76:99.
3. Schmidtke K, Büttner-Ennever JA. Nervous control of eyelid function: a review of clinical, experimental and pathological data. Brain 1992; 115:227-247.
4. Büttner-Ennever JA, Büttner U, Cohen B, Baumgartner G. Vertical gaze paralysis and the rostral interstitial nucleus of the medial longitudinal fasciculus. Brain 1982;105:125-149.
5. Johkuraa K, Komiyamaa A, Hasegawab O, Kuroiwab Y. Downgaze palsy and bilateral ptosis due to a thalamomesencephalic lesion. J Neurol Sci 1998;161:176-179.
6. Moncayo J, Bogousslavsky J. Vertebro-basilar syndromes causing oculo-motor disorders. Curr Opin Neurol 2003;16:45-50.
7. Leigh JR., Zee DS. The neurology of eye movements. 3.Ed. New York: Oxford University Press, 1999.
8. Roongroj B, Gordon T P, John LR. A hypothetical scheme for the brainstem control of vertical gaze [Medical Hypothesis]. Neurology 2000; 54:1985-1993.
9. Büttner-Ennever JA, Acheson JF, Büttner U, et al. Ptosis and supranuclear downgaze paralyis. Neurology 1989;39:385-389.
10. Maranhão-Filho PA, Pires MEP. Metastasis to the unilateral oculomotor nucleus complex: case report. Arq Neuropsiquiatr 2006;64:520-522.
11. Kong L, Lu JJ, Hu C, Guo X, Wu Y, Zhang Y. The risk of second primary tumors in patients with nasopharyngeal carcinoma after definitive radiotherapy. Cancer 2006;107:1287-1293.
12. Modan B, Mart H, Baidatz D, Steinitz R, Levin SG. Radiation-induced head and neck tumours. Lancet 1974;1:277-279.
13. Benbassat CA, Olchovsky D.Prolactinoma and other head and neck tumors after scalp irradiation. J Surg Oncol 1992;50:270-273.
14. Juven Y, Sadetzki S. A possible association between ionizing radiation and pituitary adenoma: a descriptive study. Cancer 2002;95:397-403.
15. Chung CK, Stryker iA, Cruse R, Vannuci R, Towfighi. Glioblastoma multiforme following prophylactic cranial irradiation and intrathecal methotrexate in a child with acute lymphocytic leukemia. Cancer 1981;47:2563-2566.
16. Shore RE, Albert RE, Pasternack BS. Follow-up study of patients treated by X-ray epilation for Tinea capitis; resurvey of post-treatment illness and mortality experience. Arch Environ Health 1976;31:21-28.
17. Spallone A, Gagliardi FM, Vagnozzi R. Intracranial meningiomas related to external cranial irradiation. Surg Neurol 1979;12:153-159.
18. Yap J, Chuba PJ, Thomas R, et al. Sarcoma as a second malignancy after treatment for breast cancer. Int J Radiat Oncol Biol Phys 2002;52:1231-1237.
19. Bruce J, Allen W, Senatus PB. Astrocytoma. eMedicine. http://www.emedicine.com/med/topic2693.htm. August 7, 2006.
20. Neglia JP, Meadows AT, Robison LL, et al. Second neoplasms after acute lymphoblastic leukemia in childhood. N Engl J Med 1991;325:1330-1336.
21. Salvati M, Polli FM, Caroli E, Frati A, Missori P, Delfini R. Radiation-induced schwannomas of the nervous system: report of five cases and review of the literature. J Neurosurg Sci 2003;47:113-116.