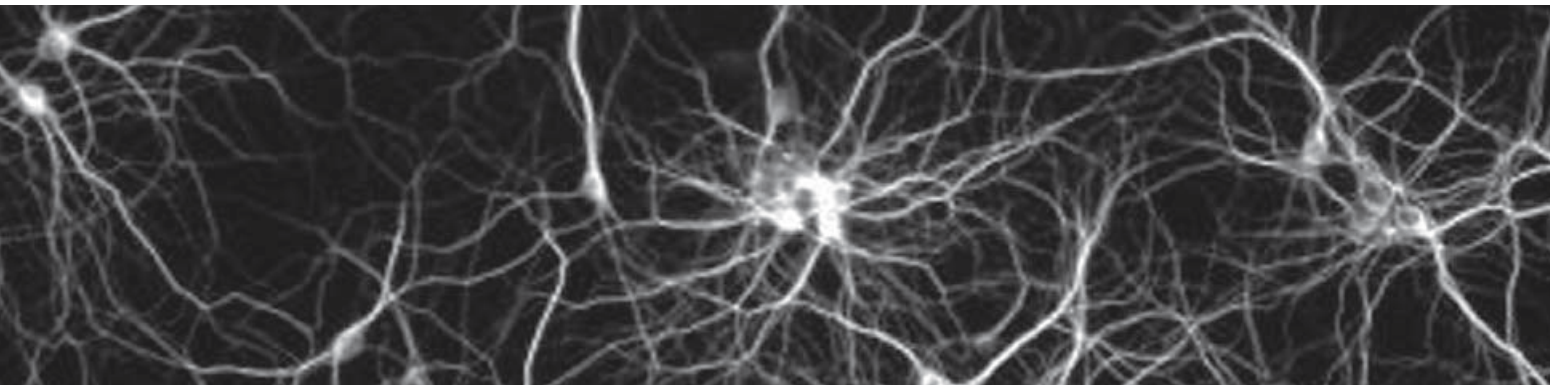

Upbeat nystagmus due to medullary lesion: case report and literature review

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ABSTRACT – Upbeat nystagmus (UBN) occurs as a consequence of disturbance in the cerebello-brainstem network responsible for the control of vertical gaze stability. Lesions responsible for UBN can be found from thalamus to caudal medulla, but are predominantly located in pons or medulla. Over the last 40 years, there have been a relatively small number of reports on patients with UBN resulting from magnetic resonance imaging, computed tomography or pathologically confirmed lesion in medulla oblongata. We report on a patient with UBN as a consequence of demyelinating lesion in medulla oblongata and review all reported cases of this clinico-anatomical association. A more detailed clinical and paraclinical approach to every patient with UBN could possibly provide us with enough information to complete this functional anatomy puzzle.

Key words: upbeat nystagmus, medulla oblongata

INTRODUCTION

Although there have been a number of reports on upbeat nystagmus (UBN), its pathophysiological mechanism still needs to be elucidated. We report on a patient with UBN as a consequence of demyelinating lesion in medulla oblongata and review all reported cases of this clinico-anatomical association.

CASE REPORT

A 53-year-old woman was admitted to our neurology department because of vertigo and unsteady gait. The symptoms started a day before admission, and were constant. The patient vomited three times that day. During neurological examination, primary position upbeat nystagmus (supplementary video) and mild left-sided dysmetria were noted. The

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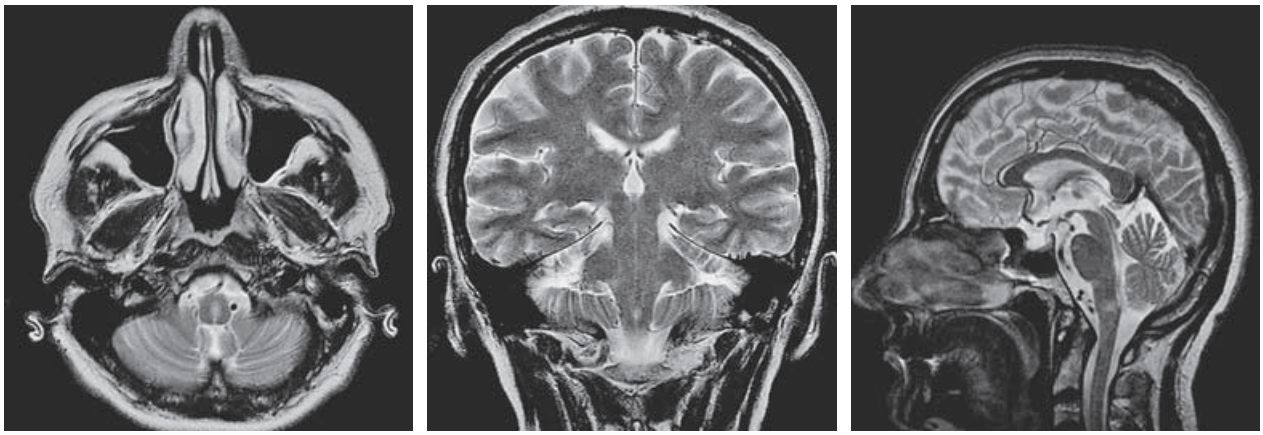

Fig. 1. *Brain MRI: (a) transverse, (b) coronal, and (c) sagittal sections showing demyelinating lesion in medulla oblongata.*

gait was atactic and tandem walk could be performed only with assistance. She reported a sense of tingling in both arms and legs, spreading from distal to proximal portions of extremities. The remaining neurological examination was normal. The patient had elevated blood pressure and heart arrhythmia controlled by a cardiologist. For the past 15 years, she had also suffered from chronic bilateral lumbosacral radiculopathy. Magnetic resonance imaging (MRI) revealed multiple supratentorial periventricular and subcortical demyelinating lesions and one lesion in the central part of medulla oblongata without postcontrast enhancement (Fig. 1).

Cerebrospinal fluid analysis (CSF) showed normal cell count, protein and glucose levels with positive oligoclonal bands only in the CSF. Vestibular-evoked myogenic potentials (VEMP) showed decreased amplitude of myogenic response in both sternocleidomastoid muscles (SCM) and abnormal morphology of the response only in right SCM. Prolonged P13 latency was recorded in right extraocular muscles. Considering clinical presentation and diagnostic tests, the patient was diagnosed with multiple sclerosis. She received intravenous methylprednisolone and Lioresal therapy, on which the neurological symptoms subsided. She was discharged from the hospital nine days after admission.

DISCUSSION

The main concept is that disturbances in the cerebello-brainstem network responsible for the control of vertical gaze stability produce instability resulting in UBN. Structures that could be affected are vertical gaze neural integrator, vertical vestibulo-ocular reflex pathways, or vertical smooth pursuit system (1). Lesions responsible for UBN can be found from thalamus to caudal medulla (2), but are predominantly located in pons or medulla (1,2). Kim *et al*. (2) divided medullary lesions into lateral, medial and lower (or caudal) groups. Lateral lesions may affect vestibular nuclei producing various types of spontaneous nystagmus and medial lesions could encompass decussating fibers of medial longitudinal fasciculus (MLF) in rostral medulla leading to UBN. Caudal medulla comprises perihypoglossal nuclei, nucleus of Roller (NR) and nucleus intercalatus of Staderini (NI), one of which is thought to act as vertical position-to-velocity neural integrator, and nucleus prepositus hypoglossi (1-3). Work by some authors (1,4) provides arguments suggesting that NR is a better candidate for the role of neural integrator. Pierrot-Deseilligny *et al*. (1) have described a possible feedback loop in detail. The following description is a simplified one. In essence, NR (or NI) receives excitatory projections from superior vestibular nuclei (SVN) and projects to the flocculus *via* a probably inhibitory pathway. SVN receives inhibitory projections from flocculus and the loop is completed. SVN transmits excitatory signals to 3rd nerve motor nucleus leading to upward eye deviation. Thus, any lesion affecting NR or its afferent or efferent projections would produce slow downward deviation of the eye, due to relative hypoactivity of the upward gaze system in respect to downward system, followed by corrective fast upward motion producing UBN. In our patient, the lesion located in central medulla may have affected afferent and/or efferent projections of neural integrator (or the neural integrator itself) resulting in UBN. Over the last 40 years, there have been a relatively small number of reports on patients with UBN resulting

Table 1. *List of reports on patients with upbeat nystagmus and MRI, CT or neuropathologic confirmation of medullary lesion*

Authors (ref. no.)	*Lesion location*	*Possibly affected structures*
Tilikete *et al*. 2002 (5)	Caudal medulla - right paramedian part	-
Pierrot-Deseilligny *et al*. 2007 (25)	Caudal medulla - dorsal paramedian part	NI, NR, nucleus paraphales
Saito *et al*. 2010 (6)	Dorsal medulla	NI
Hojin Choi *et al*. 2011 (7)	Dorsal medulla	NI, perihypoglossal nuclei
Hirose *et al*. 1998 (3)	Unilateral medial medullary lesion	NI
Munro *et al*. 1993 (12)	Left central part of medulla	NI
Roh and Lee 1996 (8)	Bilateral medial lesion in rostral medullary tegmentum	-
Adamec *et al*. 2011 (9)	Caudal medulla	NI
Janssen *et al*. 1998 (10)	Caudal medulla - dorsal paramedian part	NI
Rousseaux *et al*. 1991 (11)	Postero-medial part of medulla	NI, nuclei prepositi hypoglossi
Kim *et al*. 2006 (2)	Two patients with lateral medulla lesion, four with medial medulla lesions, and two with lower medulla lesions	-
Kim *et al*. 2012 (13)	Caudal dorsomedial medulla	NI, NR
Choi *et al*. 2004 (14)	Rostral paramedian medulla	Crossing pathways from the bilateral anterior semicircular canal
Larner *et al*. 1998 (4)	Caudal medulla - dorsal paramedian part	NI
Hendrix *et al*. 1992 (15)	Chiari-I malformation	-
Chait and Barber 1979 (16)	Chiari-I malformation	-
Kumar *et al*. 2002 (17)	Chiari-I malformation (4 patients)	-
Kanaya *et al*. 1994 (18)	Postero-medial part of medulla	Nuclei prepositi hypoglossi
Lee *et al*. 1992 (19)	Paramedian medulla	-
Kim *et al*. 1995 (20)	Two patients with medial medullary infarction	-
Ohkoshi *et al*. 1998* (21)	Caudal medulla	Demyelinating lesions in white matter surrounding the hypoglossal nuclei, NI, and MLF
Gilman *et al*. 1977* (22)	-	Low grade cellular astrocytoma infiltrating MLF bilaterally, nuclei prepositi hypoglossi and all vestibular nuclei
Keane *et al*. 1987* (23)	Patient 1 - symmetric destruction of midline medullary structures Patient 2 - medial medulla	Patient 1 - NR, NI, MLF bilaterally Patient 2 - NR, MLF bilaterally
Elliott *et al*. 1989 (24)	Four medulloblastoma survivors	-

NI, nucleus intercalatus of Staderini; NR, nucleus of Roller; MLF, medial longitudinal fasciculus;
*denotes neuropathological studies

from MRI, computed tomography, or pathologically confirmed lesion in medulla oblongata. Table 1 summarizes data from these reports.

A more detailed clinical and paraclinical approach to every patient with UBN may provide us with enough information to complete this functional anatomy puzzle.

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