Involvement of peripheral IIIrd nerve during MS: report of a new case and discussion of the underlying mechanism.

Natalia Shor¹, Maria del Mar Amador², Didier Dormont^{1,3},
Catherine Lubetski², Anne Bertrand^{1,3}

Affiliations:

¹ AP-HP, Hôpital de la Pitié-Salpêtrière, Service de Neuroradiologie Diagnostique et Fonctionnelle, F-75013, Paris, France

² AP-HP, Hôpital de la Pitié-Salpêtrière, Service de Neurologie, F-75013, Paris, France

³ Inserm U1127, CNRS UMR 7225, Sorbonne Universités, UPMC Univ Paris 06 UMR S 1127, Institut du Cerveau et de la Moelle épinière, ICM, Inria Paris-Rocquencourt, F-75013, Paris, France

Keywords:

Multiple sclerosis, peripheral neuropathy, cranial nerve, cisternal enhancement.

Corresponding author

Anne Bertrand

Service de Neuroradiologie Diagnostique et Fonctionnelle

Hôpital de la Pitié-Salpêtrière

47/83 boulevard de l'Hôpital 75013 PARIS

Phone: + 33 1 42163596

Fax: + 33 1 42163515

Email: anne.bertrand@aphp.fr

Abstract:

Multiple sclerosis (MS) is a chronic disorder that affects the central nervous system myelin. However, a few radiological cases have documented an involvement of

peripheral cranial nerves, within the subarachnoid space, in MS patients. We report the case of a 36-year-old female with a history of relapsing remitting (RR) MS who consulted for a subacute complete paralysis of the right IIIrd nerve. MRI examination showed enhancement and thickening of the cisternal right IIIrd nerve, in continuity with a linear, mesencephalic, acute demyelinating lesion. Radiological involvement of the cisternal part of IIIrd nerve has been reported only once in MS patients.

Radiological involvement of the cisternal part of Vth nerve occurs more frequently, in almost 3% of MS patients. In both situations, the presence of a central demyelinating lesion, in continuity with the enhancement of the peripheral nerve, suggests that peripheral nerve damage is a secondary process, rather than a primary target of demyelination.

Case report:

We report the case of a 36-year-old woman with an 18-year history of RR MS. She has been treated by interferon for the last 4 years, without any clinical relapse or MRI activity. The last relapse in 2010 left her with an Expanded Disability Status Scale (EDSS) of 2.0 due to sensory deficit of the lower limbs. In November 2015, she presented with a painless binocular vertical diplopia associated with right upper eyelid ptosis. Clinical examination revealed a complete palsy of the right IIIrd nerve (Figure 1A-D), with a vertical misalignment of the eyes in primary gaze, a limitation of elevation, adduction and depression of the right eye and a discrete enlargement of the right pupil. Visual acuity was normal for both eyes. There was no other new neurological deficit. Brain MRI showed a small, T2 Fluid Attenuated Inversion

Recovery (FLAIR) hyperintense, contrast-enhanced mesencephalic lesion compatible with acute demyelination (Figure 2A-C, arrowheads). This lesion was located at the inner side of the right cerebral peduncle, next to the root exit zone (REZ) of the right IIIrd nerve, which was enlarged and enhanced after contrast injection, from the REZ to the cavernous sinus (Figure 2A-C, arrows). MRI also demonstrated multiple demyelinating lesions of the corpus callosum and deep white matter (Fig 2D) without any post-gadolinium enhancement. The carotid arteries had a normal appearance (not shown). There was no compressive lesion on the right IIIrd nerve. The patient was treated by intravenous methylprednisolone (1g/day for 3 days) with a complete recovery of symptoms within 2 months of onset.

Discussion:

MS is characterized by a demyelination of the central myelin, produced by oligodendrocytes. Thus, MS lesions should not affect peripheral cranial nerves, as they contain peripheral myelin produced by Schwann cells. Only one other case of radiological involvement of peripheral, cisternal IIIrd nerve in MS has been reported in the English-language literature (1). As in our case, there was a demyelinating lesion located in the cerebral peduncle, close to the emergence of the IIIrd nerve, with continuity between the enhancement of the demyelinating lesion and the enhancement of the cisternal IIIrd nerve. In both cases, the IIIrd nerve paresis was complete, with both intrinsic and extrinsic involvement. In our case however, pupillary involvement was relatively mild, which was not in favor of an extrinsic compression, rather suggesting an intrinsic damage of the IIIrd nerve. Cisternal IIIrd nerve enhancement

has been reported in other conditions, including infectious meningitis (tuberculosis, Lyme disease), carcinomatous meningitis, lymphoma and leukemia. Cisternal IIIrd nerve enhancement related to MS is exceptional, however, cisternal enhancement has been frequently observed in the Vth nerve in MS patients (2,8-2,9% of cases) (2,3). This radiological finding was not associated with trigeminal neuralgia, but sometimes (37.5%) with painless paresthesia of the V3 territory (4). Interestingly, when T2-weighted sequences were available (3,4) an ancient (non-enhancing) or recent (contrast-enhancing) linear pontine demyelinating lesion was always noted, in continuity with the emergence of the affected Vth nerve. Some authors have suggested that such enhancement of the peripheral Vth nerve in MS patients may reflect a demyelinating process specifically targeting the peripheral myelin (2,4). Indeed, the transition zone between central and peripheral myelin of the Vth nerve is located less than 7 mm from the REZ (5); thus, an enhancement throughout the entire length of the cisternal Vth nerve does reflect an involvement of the peripheral myelin. However, the constant presence of an adjacent intrapontine lesion, when T2-weighted images were analyzed, suggests that this involvement of peripheral myelin may correspond to a point-to-point extension of the inflammatory reaction, rather than a specific peripheral myelin demyelination process. This extension may be driven by a mechanical progression of edema along the cranial nerves, or by the propagation of inflammatory changes along the venous structures adjacent to the cranial nerves. The fact that some patients present with an enhancement of the peripheral Vth nerve, while the adjacent central demyelinating lesion does not enhance, suggests that inflammatory changes may persist longer in the peripheral nerve than in the CNS (4)

A late occurrence of hypertrophy of the Vth nerve, without contrast enhancement, in patients with long-lasting MS (3), may reflect an efficient remyelination process within the peripheral nerve. Interestingly, trigeminal enhancement is more frequent in secondary progressive MS patients, which could be explained by the greater dissemination and duration of the disease (4).

Conclusion:

We report the second case of radiological involvement of cisternal peripheral IIIrd nerve in an MS patient. Radiological involvement of a cisternal cranial nerve in MS patients is exceptional for the IIIrd nerve, but has been reported more frequently for the Vth nerve. Given the constant association with an adjacent central lesion on T2-weighted images, we suggest that such involvement of cisternal peripheral cranial nerve in MS reflect a local propagation of inflammatory changes, rather than a specific targeting of the peripheral myelin

Acknowledgements:

We thank the patient who gave consent for us to write about her case.

References

1. Bhatti MT, Schmalfuss IM, Williams LS, Quisling RG. Peripheral third cranial nerve enhancement in multiple sclerosis. *AJNR Am J Neuroradiol.* 2003 Aug;24(7):1390–5.

2. Van der Meijs AHC, Tan IL, Barkhof F. Incidence of enhancement of the trigeminal nerve on MRI in patients with multiple sclerosis. *Mult Scler*. 2002;8(1 suppl):64–7.
3. Pichiecchio A, Bergamaschi R, Tavazzi E, Romani A, Todeschini A, Bastianello S. Bilateral trigeminal enhancement on magnetic resonance imaging in a patient with multiple sclerosis and trigeminal neuralgia. *Mult Scler Houndmills Basingstoke Engl*. 2007 Jul;13(6):814–6.
4. Da Silva C, da Rocha A, Mendes M, Maia A, Braga F, Tilbery C. Trigeminal involvement in multiple sclerosis: magnetic resonance imaging findings with clinical correlation in a series of patients. *Mult Scler*. 2005 Jun 1;11(3):282–5.
5. Peker S, Kurtkaya O, Uzün I, Pamir MN. Microanatomy of the central myelin-peripheral myelin transition zone of the trigeminal nerve. *Neurosurgery*. 2006 Aug;59(2):354–359; discussion 354–359.