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Case report

Clinical and radiological findings of facial paralysis in multiple sclerosis

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ABSTRACT

Background: Diagnosis of central or peripheral facial palsy (FP) is traditionally based on clinical evaluation. This study aims at investigating the relationship between clinical evaluation of FP and lesion location as visible on Magnetic Resonance Imaging (MRI) in patients with Multiple Sclerosis (MS) for the purpose of adding supporting evidence to the diagnosis of central or peripheral FP in these patients.

Methods: A retrospective study was conducted on data from patients who underwent MS treatment between January 2016 and January 2019 at the MS Center of Wayne State University, MI, USA, and presented with at least one episode of FP during the observational period. The following data was collected from each patient: demographics, time from MS onset, side of FP, FP type (central or peripheral, as clinically evaluated), FP onset, FP treatment, amount of recovery of normal facial movements, time elapsed from beginning of FP treatment, number of FP recurrences, lesions presence/absence and location as visible on MRI. Correlation analysis was performed to assess to which extent clinical evaluation of FP correlated with presence of MRI lesions in different locations.

Results: Eighteen patients were included in this study. In thirteen patients (72.2%) FP was classified as peripheral. Among them only five (38.4%) displayed one or more lesions in the pons. Correlation between presence of lesions in the pons and presence of peripheral FP was statistically significant ($p = 0.02$). Correlation between presence of lesions in the cortex (observed in 61.5% of patients with FP clinically evaluated as peripheral) and presence of FP clinically evaluated as peripheral was also statistically significant ($p = 0.01$). Finally, presence of lesions in the cortex was significantly correlated with presence of FP clinically evaluated as central ($p = 0.02$).

Conclusions: FP clinically classified as peripheral may be caused by central lesions in the cortex or pons and not only by peripheral facial nerve damage. In MS patients, FP may appear at the onset of the disease and be misdiagnosed as Bell 's palsy. Clinicians should carefully approach FP diagnosis and perform a brain as well as temporal bone MRI before pursuing pharmacological treatment.

1. Introduction

Multiple sclerosis (MS) is a chronic neurodegenerative, inflammatory, demyelinating disease (Calabresi 2004). In MS, lesions are typically confined to the Central Nervous System (CNS) (Kwon et al., 2008) and there is very limited evidence of involvement of the peripheral system (Krieger et al., 2016; Vogt et al., 2009). In MS patients who present with otolaryngologic symptoms (Di Stadio and Ralli 2018; Ralli et al., 2018; Di Stadio and Bernitsas 2019), these symptoms may stem from a central involvement of auditory (Di Stadio et al. 2018a), vestibular (Di Stadio et al. 2018b), or facial pathways (Critchley 2004; Di Stadio and Bernitsas 2018). With a prevalence of 7%, facial palsy (FP) is commonly observed in MS patients by ear, nose, and throat specialists (Di Stadio and Bernitsas 2019). When a widespread lesion affects cochlear and vestibular nuclei, which are close to the facial nuclei, the patient may present with additional symptoms such as vertigo or hearing impairment (Di Stadio et al. 2018a; Di Stadio et al. 2018b).

While in MS patients FP may arise from lesions in either central or peripheral pathways, pinning down the actual origin of FP via clinical examination in these patients is a particularly complex and prone to errors task. Clinically, FP is labeled of central origin if it affects the

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muscles of the II and III of the face (zygomatic, orbicularis oris, buccinator, mentalis, and platysma) (Di Stadio 2015) and of peripheral origin if it affects all facial muscles. Thus, it is well known that FP of central origin is caused by lesions above the level of the facial nucleus (in the pons -which belongs to the brainstem- of the contralateral hemisphere or in the cortex) and FP of peripheral origin is caused by lesions of the ipsilateral facial nerve, usually at the level of the geniculate ganglion (located in the facial canal). Unfortunately, such a definition of central and peripheral FP captures only marginally what is observed in MS patients. In fact, patients who present with FP clinically defined as peripheral can display lesions in areas of the CNS not extending to the root entry zone (REZ) (Kwon et al., 2008; Fukazawa et al., 1997 , Ivankovic and Demarin 2011), for example at the level of the ipsilateral facial nucleus or in the facial nerve at the level of the pons (Gilden 2004) . Such limitations in the clinical definition of FP have implications in clinical practice. For example, based on the above clinical definition, a FP that is clinically diagnosed as peripheral but in fact is caused by a lesion in the CNS may be misdiagnosed as Bell's Palsy (BP) (a condition caused by damage in the peripheral facial nerve, which is typically treated with corticosteroids without having the patient undergo magnetic resonance imaging (MRI)). The fact that BP typically resolves with corticosteroid treatment, which is also the standard treatment for relapsing MS, further contributes to misdiagnosis.

This study aims at investigating the relationship between FP types as clinically evaluated and underlying MS lesion locations. Specifically, we aimed at investigating whether in MS patients presenting with FP, MRI can help uncover the origin of FP. To this end, we enrolled 18 MS patients who presented with FP (primary and recurrent). We examined and compared clinical findings (supporting either a central or peripheral origin of FP) with MRI results.

2. Materials and method

This retrospective, case series study was conducted at the MS Center of the Wayne State University, Detroit, USA and was approved by the local Institutional Review Board (IRB). Informed, written consent was obtained from all study participants.

Clinical records of patients under MS treatment between January 2016 and January 2019 were reviewed and patients who presented with at least one episode of FP were selected. The MS diagnosis was performed following the McDonald 2010 diagnostic criteria (Polman et al., 2011).

The diagnosis of FP was initially based on clinical observation only and was not supported by MRI findings. Namely, the FP was labeled as “central” if the paralysis involved the middle/low part of the face and “peripheral” if the paralysis affected all muscles of the hemiface.

The following data was collected for each patient: demographics, time from MS onset, side of FP, FP type (central or peripheral, as clinically evaluated), FP onset (which was defined as “early” when FP presented early on in the disease among the initial MS symptoms and as “late” when FP presented later in a patient with a known history of MS), FP treatment, amount of recovery of normal facial movements as measured by the ADS scale (Di Stadio 2015), time elapsed from the FP treatment, and number of FP recurrences.

A 1.5 Tesla brain and temporal bone MRIs (Philips Medical System Achieva scan, Philips, Best, the Netherlands) was acquired from each patient. Analysis of T2 MRI sequences was performed by a neuroradiologist and aimed at identifying the presence/absence of lesions and their location. In patients with known history of MS, the most recent MRI was compared with the previous MRI scans to assess if new lesions were present.

2.1. Statistical analysis

A Chi (χ)-square test was used to assess the correlation between presence of lesions in the pons and presence of clinically defined peripheral FP. Similarly, a χ-square test was used to assess the correlation between presence of lesions in the cortex and presence of peripheral FP and between presence of lesions in the cortex and presence of central FP. The level of significance for all tests was set to 0.05. All analyses were performed with Stata ®.

Table 1
The table summarizes the patients' demographics and MS features.

Patient #	Sex	Age	Type of MS	Years of illness
1	**F**	24	**RR**	just diagnosed
2	**F**	48	**RR**	12
3	**M**	61	**SP with relapses**	24
4	**F**	33	**RR**	4
5	**F**	52	**SP with relapses**	17
6	**F**	36	**RR**	3
7	**M**	56	**PP**	7
8	**F**	42	**RR**	8
9	**M**	39	**RR**	10
10	**F**	44	**RR**	3
11	**F**	38	**RR**	4
12	**M**	55	**SP with relapses**	16
13	**M**	42	**RR**	17
14	**F**	58	**RR**	20
15	**M**	59	**RR**	15
16	**F**	62	**RR**	15
17	**M**	56	**RR**	27
18	**F**	49	**RR**	21

3. RESULTS

3.1. Demographics

The data from $N = 18$ patients ($N = 11$ females and $N = 7$ males; average age 47.4 years, standard deviation (SD) 10.8 years; time from MS onset 12.3 years, SD 7.9 years (CI 95%: 0–27)) were analyzed. All patients suffered from at least one episode of FP (central or peripheral) during the observational period. One patient suffered from primary progressive (PP) MS (5.5%), three from secondary progressive (SP) MS with relapses (16.6%), and 14 from relapsing remitting (RR) MS (Table 1).

3.2. Facial palsy

The left side was the most affected side of the face (11 out of 18 patients presented with left FP). In five patients, FP was clinically diagnosed as of central origin (27.7%) (cFP) and in 13 as of peripheral origin (72.3%) (pFP). Among patients with pFP, none presented any symptom other than alteration of facial motility; also, pFP severity score was lower than 5 as measured by the ADS scale. Specifically, one patient (7.7%) had a score of 4.7; five patients (38.4%) had a score between 1.5 and 3.9 (2.34 $\pm$ 0.93); and seven patients (53.9%) had a score between 0 and 1.2 (0.6 $\pm$ 0.4). Among all patients, in 4 patients (27.7%) FP onset was early (in one patient FP presented during the first year from the MS diagnosis and in three patients FP was the only presenting symptom of MS) . In 14 patients (72.3%), the FP onset was late (at least two years after their MS diagnosis). Among the patients with early FP onset, 3 were clinically diagnosed with pFP (Fig. 1) and 1 with cFP; among the patients with late FP onset, 4 were clinically diagnosed with cFP and 10 with pFP. In the latter patients, demyelinating lesions spread in the brain (Table 2) were present, which were not visible in their previous MRI.

In the three patients in whom FP was the presenting symptom of MS (patient 1, 6, and 8), FP showed the typical clinical signs of pFP, i.e. hemifacial palsy affecting all the muscles of the three facial districts (upper, middle and low face) (Di Stadio 2016). pFP severity was 0 for patient 1, 0.9 for patient 6, and 1.2 for patient 8 as measured by the

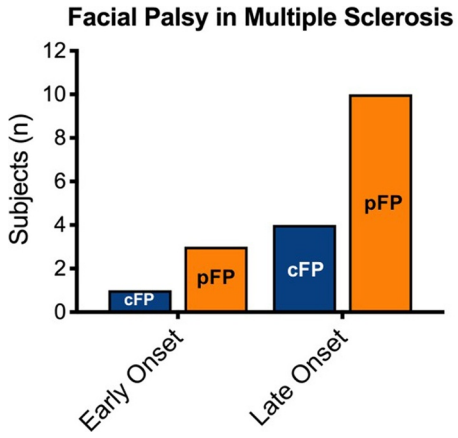

Fig. 1. The image shows the prevalence of the different clinical aspect (peripheral o central) in case of early (as presenting symptom) or late onset of MS.

ADS score (see Table 2, in bold).

The FP as presenting symptom was initially diagnosed as stroke sequelae in one patient (cFP), and as Bell's palsy (BP) in three patients (16.7%) (pFP).

In all patients, FP (cFP and pFP) was treated with a high dose of oral corticosteroids for 10 consecutive days. Most patients ($N = 14$) completely recovered within 6 months, and four (3 with cFP and 1 with pFP) only partially recovered (Fig. 2) and still displayed facial asymmetry 12 months after the FP onset.

Twelve patients (66.7%, 3 with cFP and 9 with pFP) suffered from a single episode of FP while in six patients (2 with cFP and 4 with pFP) FP recurred; in 4 of them (66.6%) FP always recurred on the same side of the first event and in 2 patients (33.4%) FP recurred on the opposite side (Fig. 3A and B).

3.3. MRI analysis

All patients presented with white matter lesions in the brain. None of the patients showed a hyperintense signal in the facial nerve tract from the ponto-cerebellum angle (APC) to the stylomastoid foramen (indicative of a peripheral facial nerve involvement) in the temporal MRI. Table 2 summarizes lesions location as visible in the MRI and type of FP as clinically evaluated.

Six patients (33.3%) displayed a pontine lesion (Fig. 4); in five of them FP was clinically evaluated as pFP and in one patient as cFP

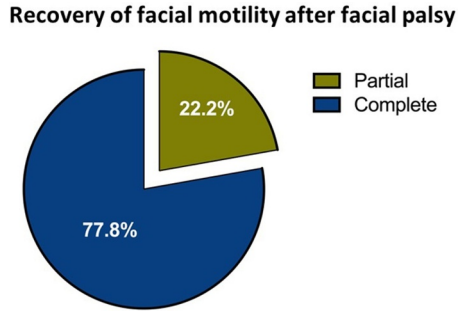

Fig. 2. The image shows the prevalence of patients who partially or completely recovered their facial movements within 6 months after the onset of FP.

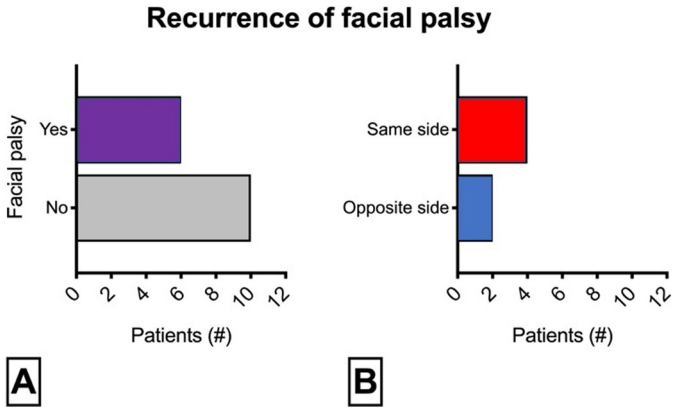

Fig. 3. Panel A) Most of our patients presented with a single episode of FP during the observational period. Panel B) When FP recurred, it typically re-occurred on the same facial side of the first episode.

(Fig. 1). In 9 patients (50%) the lesions were observed only in the cortex with no involvement of the brainstem (Fig. 5); in 7 of them (77%), FP was clinically diagnosed as pFP and in 2 (23%) as cFP. Three patients (16.6%) had lesions both in the cortex and brainstem; in 2 of them FP was clinically evaluated as cFP and in one as pFP.

3.4. Correlation

Among the thirteen patients suffering from pFP as clinically diagnosed, only five (38.4%) displayed a lesion in the pons, which

Table 2
Distribution of the lesions in the different part of CNS in our data sample. Patients who presented with FP as initial and only symptom of MS are in b.

Patient#	Type and side of FP		Lesion locations (from MRI)
	Central	Peripheral	
1		**Left**	**Left side of pons**
2		Left	Left side of pons
3		Right	Right side of pons
4		Left	Diffused in the cortex, not involving brainstem
5	Right		Diffused in cortex and brainstem
6		**Right**	**Right side of midbrain and pons (small lesion)**
7		Left	Left side of cortex, not involving brainstem
8		**Left**	**Left side of subcortex only, not involving brainstem**
9		Left	Diffused cortex and brainstem
10	Right		Diffused in cortex, not involving brainstem
11		Left	Left side of pons
12		Left	Left side of subcortex, not involving brainstem
13	Left		Left side of cortex (para atrial occipital)
14	Right		Left side of pons (tegmen) and brainstem (paraoccipital)
15		Left	Diffused in cortex (periventricular) and hypotrophy of corpus callosusm
16		Left	Diffused in cortex (iuxatacortical) with nuclei involvement(semioval and centromedullar)
17	Right		Diffused in cortical nuclei (semioval and periventricular), cerebellum, and brainstem
18		Right	Diffused in cortex (priventricular)

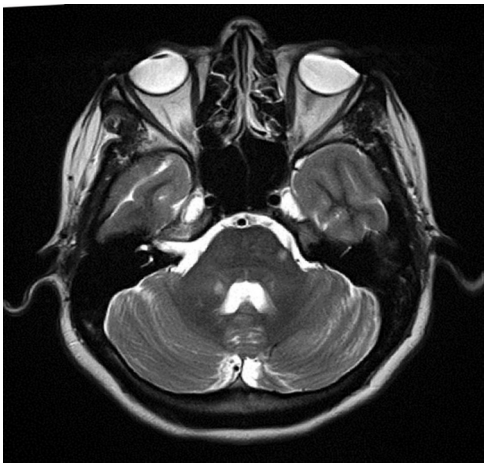

Fig. 4. MRI of a patient that presents pons lesion with a clinically peripheral facial palsy.

anatomically correlated with the side of the FP; the correlation between presence of lesion(s) in the pons and presence of pFP was significant (χ: $p = 0.02$). Additionally, presence of lesion(s) in the cortex (observed in 61.5% of patients with pFP) was significantly correlated with presence of pFP ($p = 0.01$). Finally, presence of lesion(s) in the cortex was highly correlated with presence of cFP ($p = 0.02$).

4. Discussion

This study analyzed the relationship between clinical features of FP and lesions location as visible on MRI in MS patients. We found that FP clinically diagnosed as pFP (13 out of 18 in our sample) occurred in MS patients who displayed demyelinating lesions not only in the pons (38.4% of cases) but also in other parts of the CNS (cortex with or without brainstem involvement). We also found that FP clinically diagnosed as cFP occurred in MS patients who displayed lesions in the cortex only; only one patient who presented with this FP type displayed demyelinating lesions just in the pons.

Interestingly, we found that presence of pFP was significantly correlated both with presence of lesions in the cortex ($p = 0.01$) and with presence of pontine lesions ($p = 0.02$). In addition, there was a correlation between presence of cFP and presence of cortical lesions ($p = 0.02$).

Our findings are consistent with those of previous studies. It has been demonstrated that MS-related pFP is associated with lesions in parts of the CNS (that should cause a FP clinically defined as cFP) other than the pons (Gilden 2004) (Zandro et al. 2008). In a large retrospective study, Zadro et al. (Zandro et al. 2008) reported that only 66.7% of MS patients with pFP had at least one lesion in the brainstem, which could have explained the symptoms, while 33.3% had a lesion in other parts of the brain and none had an involvement of the facial nerve. These results suggest that a FP that shows clinical signs of a pFP, should prompt the clinician to consider that the FP may in fact be caused by lesions located in the CNS (Geurts and Barkhof 2008; Calabrese et al., 2013). Potential causes of FP that warrant considerations and are often dismissed include MS associated with lesions in the motor cortex (M1) (Di Stadio and Bernitsas 2018) and/or lesions in the pons but non-detectable by 1.5 Tesla MRI (Di Stadio et al. 2018b).

These results suggest that the traditional, clinical definition of central and peripheral FP may have limitations and should be revised. Sajadi et al. (Sajadi et al., 2011) also previously highlighted such limitations and suggested that the definition of cFP and pFP originally proposed by Razi (Shoia et al., 2009) should be used and emphasized that additional symptoms should always be considered besides the MRI findings in order to correctly understand the oigin of FP. In MS, this method is particularly useful as FP is typically associated with a number of other symptoms, for example hearing or vestibular disorders (Di Stadio and Ralli 2018; Di Stadio et al. 2018a). On the other hand, presence of multiple symptoms can make the diagnostic process challenging especially when patients are seen for the first time. In our sample, misdiagnosis occurred in 21.7% of cases; specifically, in 5% of cases FP was attributed to stroke and in 16.7% to BP as opposed to MS. As highlighted by Saleh et al., misdiagnosis may delay treatment of the primary disease (in this case, MS) thereby increasing the risk of disability (Saleh et al., 2016). In MS patients with FP, demyelinating lesions can spread in the language pathway causing speech difficulties (Nordio et al., 2018), which may lead the clinician to attribute the FP to a stroke as opposed to MS. Patients with FP and large MS demyelinating lesions in the facial or cochlea-vestibular nuclei may also display

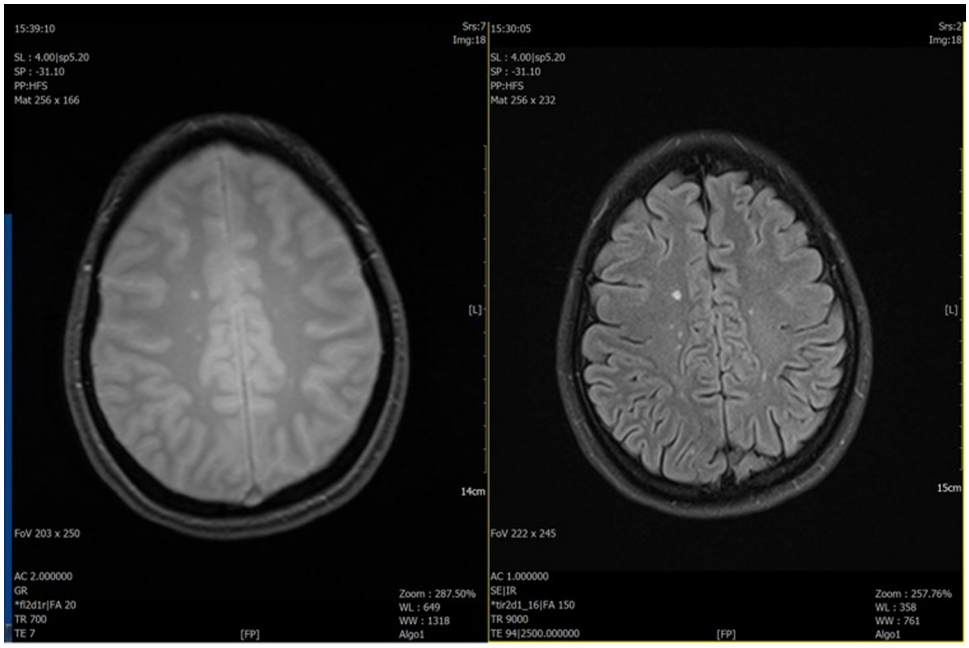

Fig. 5. MRI of a patient that has demyelinating lesions in the cortex in presence of a peripheral facial palsy.

hearing impairment or vertigo (Di Stadio et al. 2018 a; Di Stadio et al. 2018 b); this may lead the clinician to attribute the FP to a BP, which can manifest with FP and hearing impairment or dysgeusia if the tract of the facial nerve between the geniculate ganglion and the stylomastoid foramen is inflamed (Billue 1997).

Finally, in this case-series, we found that pFP was more prevalent on the left side of the face but the demyelinating lesions were spread in the cortex or in the pons equally between sides as visible on MRI. Differently from cFP, pFP recurred (37.5%) during the observational period either on the same side of the first episode or on the contralateral side; this occurred during the relapsing phases of MS, when onset of new demyelinating lesions was also visible in the MRI. This suggests that in MS patients a pFP episode should prompt the clinician to consider the FP as a sign of relapsing MS. In addition, the presence of pFP in a young healthy patient should prompt the physician to inquire about other non-specific symptoms and include MS in the differential diagnosis of FP. In the majority of cases, FP occurred later in the disease (72.3% of patients) and most patients treated with corticosteroids completely recovered.

Overall, the results of this case series suggest that in MS patients diagnosis of FP based exclusively on clinical examination is likely to be inaccurate; MS-related FP may not be recognized especially when FP is one of the first symptoms of the demyelinating disease and presents with clinical signs typical of pFP.

Our results support the idea that pFP can be related to a lesion in the brain or in the brainstem; for example, it can be due to a central demyelination as opposed to facial nerve inflammation. Because FP responds to corticosteroid treatment regardless of its origin (MS or BP) (Hohman and Hadlock 2014), prior to prescribing corticosteroids clinicians should always consider ordering an MRI . Our results should be considered preliminary and should be validated on larger data samples.

Limitations of the study: This study has several limitations. First, due to its retrospective nature, researchers were unblinded to the patients' MS diagnosis; also retrospective analysis of MRIs might have underestimated the actual patient MS severity, size and/or number of MS lesions, given that corticosteroid treatment might have reduced the size and/or number of inflamed areas. Finally, all MRI images were acquired with a 1.5 Tesla MRI which might have not detected demyelinating lesions small in size.

6. Conclusions

In MS patients, pFP may be the first presentation of the disease and be misdiagnosed as BP. Treatment with corticosteroids (without performing a brain MRI) may successfully contribute to FP recovery regardless of its origin, but may interfere with MS diagnosis, masking the underlying pathology and possibly leading to misdiagnosis. This is particularly problematic in early MS as it may delay the MS diagnosis; in late MS, FP may be indicative of a reactivation of the disease with a new brain lesion. Clinicians should carefully approach the diagnosis of pFP and perform a brain and temporal bone MRI investigation before pursuing a pharmacological treatment given that pFP may be due to a central involvement rather than being a sign of peripheral facial nerve damage. Our results are consistent with those of Saleh (Saleh et al., 2016) which, like ours, highlighted the importance of performing brain MRI to reduce the likelihood of misdiagnosis and delayed treatment of MS.

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Declaration of Competing Interest

None.

References

Billue, J.S., 1997. Bell's palsy: an update on idiopathic facial paralysis. Nurse Pract 22 (88), 97–100 102-5; quiz 106-7.
Calabresi, P.A., 2004. Diagnosis and management of multiple sclerosis. Am Fam Physician 70, 1935–1944.
Calabrese, M., Favaretto, A., Martini, V., Gallo, P., 2013. Grey matter lesions in MS: from histology to clinical implications. Prion 7 (1), 20–27. https://doi.org/10.4161/pri.22580.
Critchley, E.P., 2004. Multiple sclerosis initially presenting as facial palsy. Aviat Space Environ Med 75, 1001–1004.
Di Stadio, A., Ralli, M., 2018. Inner ear involvement in multiple sclerosis: an underestimated condition? Mult Scler 24, 1264–1265. https://doi.org/10.1177/1352458517750010.
Di Stadio, A., Bernitsas, E., 2018. The origin of facial palsy in multiple sclerosis. Otolaryngol Open J. 4 (1), e1–e4. https://doi.org/10.17140/OTLOJ-4-e006.
Di Stadio A., Dipietro L., Ralli M., Meneghello F., Minni A., Greco A., Stabile M.R., Bernitsas E.Eur rev med pharmacol sci sudden hearing loss as an early detector of multiple sclerosis: a systematic review. 2018a;22 :4611–4624. doi: 10.26355/eurrev_201807_15520.
Di Stadio, A., Dipietro, L., Ralli, M., Greco, A., Ricci, G., Bernitsas, E., 2018b. The role of vestibular evoked myogenic potentials in multiple sclerosis-related vertigo. a systematic review of the literature. Mult Scler Relat Disord 2 (8), 159–164. https://doi.org/10.1016/j.msard.2018.12.031.
Di Stadio, A., Bernitsas, E., 2019. Otolaryngological symptoms and multiple sclerosis: a forgotten and underestimated relationship. Mult Scler Relat Disord 28, 197–198. https://doi.org/10.1016/j.msard.2019.01.010.
Di Stadio, A., 2015. Another scale for the assessment of facial paralysis? ads scale: our preposition. how to use it. J Clin Diagn Res 9 (12), MC08–MC11. https://doi.org/10.7860/JCDR/2015/15366.6953.
Fukazawa, T., Moriwaka, F., Hamada, K., Hamada, T., Tashiro, K., 1997. Facial palsy in multiple sclerosis. J Neurol. 244, 631–633.
Geurts, J.J., Barkhof, F., 2008. Grey matter pathology in multiple sclerosis. Lancet Neurol 7, 841–851. https://doi.org/10.1016/S1474-4422(08)70191-1.
Gilden, D.H., 2004. Clinical practice. bell's palsy. N Engl J Med 351, 1323–1331.
Hohman, M.H., Hadlock, T.A., 2014. diagnosis, and management of facial palsy: 2000 patients at a facial nerve center. Laryngoscope Etiology 124, E283–E293. https://doi.org/10.1002/lary.24542.
Ivankovic, M., Demarin, V., 2011. From recurrent peripheral facial palsy to multiple sclerosis. Acta Clin Croat 50, 419–421.
Krieger, S.C., Cook, K., De Nino, S., Fletcher, M., 2016. The topographical model of multiple sclerosis: a dynamic visualization of disease course. Neurol Neuroimmunol Neuroinflamm 3, e279. https://doi.org/10.1212/NXI.0000000000000279.
Kwon, J.Y., Kim, J.Y., Jeong, J.H., Park, K.D., 2008. Multiple sclerosis and peripheral multifocal demyelinating neuropathies occurring in a same patient. J Clin Neurol 4, 51–57.
Nordio, S., Bernitsas, E., Meneghello, F., Dipietro, L., Palmer, K., Stabile, M.R., 2018. Can expiratory and phonation times be measures of disease severity in patients with multiple sclerosis? a pilot study. Di Stadio A. Mult Scler Relat Disord 23, 27–32. https://doi.org/10.1016/j.msard.2018.04.010.
Polman, C.H., Reingold, S.C., Banwell, B., Clanet, M., Cohen, J.A., Filippi, M., Fujihara, K., Havrdova, E., Hutchinson, M., Kappos, L., Lublin, F.D., Montalban, X., O'Connor, P., Sandberg-Wollheim, M., Thompson, A.J., Waubant, E., Weinshenker, B., Wolinsky, J.S., 2011. Diagnostic criteria for multiple sclerosis: 2010 revisions to the mcdonald criteria. Ann Neurol. 69 (2), 292–302. https://doi.org/10.1002/ana.22366. Feb.
Ralli, M., Di Stadio, A., Visconti, I.C., Russo, F.Y., Saccucci, M., Balla, M.P., Greco, A., de Vincentiis, M., 2018. Otolaryngologic symptoms in multiple sclerosis: a review. International Tinnitus Journal 22, 160–169. https://doi.org/10.5935/0946-5448.20180027.
Sajadi, M.M., Sajadi, M.R., Tabatabaie, S.M., 2011. The history of facial palsy and spasm: hippocrates to razi. Neurology 77, 174–178. https://doi.org/10.1212/WNL.0b013e3182242d23.
Saleh, C., Patsi, O., Mataigne, F., Beyenburg, S., 2016. Peripheral (Seventh) nerve palsy and multiple sclerosis: a diagnostic dilemma - A Case report. Case Rep Neurol 8 (1), 27–33.
Shoja, M.M., Tubbs, R.S., Loukas, M., Shokkouhi, G., Ardalan, M.R., 2009. Facial palsy and its management in the kitab al-Hawi of rhazes. Neurosurgery 64, 1188–1190.
Vogt, J., Paul, F., Aktas, O., Müller-Wielsch, K., Dörr, J., Dörr, S., Bharathi, B.S., Glumm, R., Schmitz, C., Steinbusch, H., Raine, C.S., Tsokos, M., Nitsch, R., Zipp, F., 2009. Lower motor neuron loss in multiple sclerosis and experimental autoimmune encephalomyelitis. Ann Neurol 66, 310–322. https://doi.org/10.1002/ana.21719.
Zadro, I., Barun, B., Habek, M., Brinar, V.V., 2008. Isolated cranial nerve palsies in multiple sclerosis. Clin Neurol Neurosurg 110, 886–888. https://doi.org/10.1016/j.clineuro.2008.02.009.