Should spinal cord MRI be systematically performed for diagnosis and follow up of multiple sclerosis? Yes

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Should spinal cord MRI be systematically performed for diagnosis and follow-up of multiple sclerosis? Synthesis

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Magnetic Resonance Imaging (MRI) has become a major tool in the diagnostic work-up of patients suspected of multiple sclerosis (MS) and in the monitoring of the disease.

Spinal cord (SC) lesions are key players in McDonald 2017 diagnostic criteria, as they correspond to one of the four anatomical locations to document dissemination in space (DIS). New or gadolinium enhancing spinal cord lesions can also be used to document dissemination in time (DIT) [1].

In parallel, while defining MS clinical course, the panel of experts recommended annual MRI scans to identify active/inactive MS in the monitoring of MS course and evaluation of disease modifying treatments [2].

In both situations, a remaining issue is to evaluate the benefit of doing a spinal cord MRI in addition to the brain imaging.

In France, the Observatoire Français de la Sclérose en Plaques (OFSEP) proposed to standardize MRI acquisitions for routine follow-up, in order to improve the monitoring of the disease. [3].

In clinical practice, there are increasing demands for MRI scaning in MS patients' care, while there are a limited number of MRI devices. Neurologists and neuroradiologists have to make decisions as to whether to scan, when to scan and how to scan spinal cord in addition to brain MRI.

Whether to scan spinal cord

Prevalence of SC lesions is around 90 % in definite MS [4; 5; 6; 7; 8]. This percentage increases up to 97 % when focal and diffuse abnormalities are included [7]. In clinically isolated syndromes (CIS), prevalence varies widely between publications, with a mean of 30 to 40 % of asymptomatic SC lesions [9; 10]. More recently, Arrambide et al. found, in the Barcelona CIS cohort, 80% of SC lesions in spinal cord presentations and 30 % in SC cord presentations [11], and Dalton et al. reported 27 % of SC lesions in optic nerve CIS [12]. Asymptomatic SC lesions were also described in radiologically isolated syndrome (RIS) with 35 % of patients presenting at least one SC lesion [13] and up to 71 % in cervical MRI when using more advanced acquisitions such as PSIR [14]. It is interesting to note that in general SC lesions are preferentially located within the cervical cord (56.4%) [7; 15]. Finally, the sensitivity of the SC lesions detection when using conventional field strengths MRI is unknown and probably underestimated. For example, when using high field MRI (4.7 T) on post mortem SC material in MS patients, 87% of white matter lesions and 73% of grey matter lesions where detected [16].

Spinal cord MRI plays also an important role in the differentiation of MS from alternative diagnosis. Rovaris et al. studied the role of SC MRI when making a diagnosis in a group of inflammatory conditions affecting the central nervous system. Spinal cord was affected in 90% in MS (n=10) versus 0% in others inflammatory diseases (systemic lupus erythematosus (n=24), Behcet's disease (n=5), Wegener's granulomatosis (n=9), antiphospholipid syndrome (n=6)) [17]. Non-specific ischaemic lesions commonly occur with aging in the brain, but not in the spinal cord [6; 18]. Consequently, a consensus of experts considered the absence of SC lesion as a minor red flag to the diagnosis of MS [19]. Moreover short-segment spinal cord lesions are highly suggestive of MS in opposition to longitudinal extensive

lesions usually evocative of other inflammatory CNS diseases (neuromyelitis optica spectrum disorders, antiMOG antibodies related disorders, acute disseminated encephalomyelitis…) [15]. Spinal cord lesions on MRI convey important diagnostic value for MS.

When to scan spinal cord

Initial workup for the diagnosis

Up to now, there was a general agreement that spinal cord MRI was not mandatory for the diagnosis of MS. Currently indications for spinal cord imaging in patients suspected of MS include: 1) any CIS patients presenting with spinal cord symptoms to rule out alternative cord pathology, 2) any CIS patient, including optic neuritis, not fulfilling McDonald criteria for DIS with the unique brain MRI , 3) patients with vascular risk factors or vascular brain MRI lesions, 4) suspicion of primary progressive MS and 5) radiologically isolated syndrome [1; 20; 21]. These indications leave out CIS cases where there is no clinical suspicion of cord involvement at onset, and when brain MRI is sufficient to full DIS criteria.

During the initial workup, brain and spinal cord MRI are the most useful paraclinical tests to achieve the diagnosis of MS.

In case of typical CIS or relapsing remitting presentation, DIS is confirmed when symptomatic or non-symptomatic lesions are found in two of the following four regions: juxtacortical, periventricular, infratentorial or spinal cord. When demonstrating DIS, spinal cord imaging slightly increases by 8% the diagnosis in patients with clinically isolated optic neuritis at baseline [12]. More recently a study on non spinal cord CIS patient showed that the number of SC scans needed to diagnose one additional patient was 7 [10].

Elsewhere, diagnosing primary progressive MS, DIS is fulfilled when 2 of the 3 following criteria are present: ≥1 T2 brain lesions characteristic of MS, ≥ 2 T2 spinal cord lesions and presence of CSF-specific oligoclonal bands [1].

In terms of DIT, the value of follow-up spinal cord imaging seems limited, since new (gadolinium-enhanced) lesions are not so frequent and the contribution of active spinal cord lesions relative to repeat brain MRI is probably very low. When demonstrating DIT, spinal cord imaging didn't improve the capacity of MS diagnosis [12; 22; 23]. Thus whole spinal cord MRI is recommended to meet DIS criteria, whereas it has a limited role for DIT in the initial workup [23].

Initial workup for the prognosis

Presence of SC lesions is predictive for conversion to clinically definite MS, especially in patients with non-spinal cord CIS who do not fulfill brain MRI criteria [10]. The presence of SC lesions increased MS risk 2.0–2.6 times independently of factors like brain lesions. If considering lesion number, the risk ranged from 1.6 to 2.1 for one lesion to 2.4–3.3 for more than 2. Spinal cord lesions increased the short-term disability risk around fivefold. Spinal cord lesions showed very high sensitivity for a shorter time to EDSS $\geqslant$3.0 [11; 24]. Furthermore a recent study on CIS patients enhanced that spinal cord

lesions were independently associated with secondary progressive multiple sclerosis at 15 years (odds ratio 4.71, P < 0.01) [25].

Spinal cord lesions are associated with increased risk of becoming symptomatic in RIS patients [13; 26]. They were particularly linked to a progressive course as 100% of RIS evolving to PPMS had spinal cord compared to 64% of those who developed CIS/MS and 23% of those who remained asymptomatic [27].

Furthermore, patients with a symptomatic or asymptomatic spinal cord lesion have a higher risk of disability accumulation than patients with a single symptomatic brainstem lesion [28].

Monitoring of the disease

As far as monitoring of MS patient, experts agree to perform annual MRI evaluations to assess disease activity [Lublin, 2013]. Annual brain MRI is recommended for RRMS patients [29]. However, as there is a strong correlation between brain and spinal cord MRI activity, annual spinal cord imaging is not recommended [2; 21]. Indeed, in a monthly follow up of 10 patients RR MS over one year, imaging of the brain alone detected 90% of the active lesions versus 10 % for the spinal cord MRI. In this study, if the patients presented brain clinical symptoms, there was no contribution of an additional spinal cord MRI. Likewise, the few cases with a spinal cord MRI activity presented medullar symptoms. Thus SC MRI is not recommended is routine MRI follow-up. SC MRI is recommended in case of SC symptoms and in case of secondary progressive evolution. Nevertheless special consideration should be given to patients with a medullar tropism of inflammation.

How to scan spinal cord

At the initial workup, an imaging of the whole spine in a sagittal plane is generally performed. However whole spinal cord imaging with T2-weighted and T1-weighted sequences may lead to false-negative and false-positive interpretations. Thus different strategies are suggested to improve specificity and sensitivity of lesion detection.

Spinal cord MRI should be performed on systems with minimum field strength of 1.5 T, with a slice thickness of 3 mm [21] and should be performed during a dedicated time, independently from the brain MRI. Indeed it is important to obtain initial high quality spinal cord images.

MAGNIMS consensus guidelines, for spinal cord lesion identification includes a combination of two sets of sagittal images with different contrasts: T2-weighted FSE, short tau inversion recovery (STIR), proton density-weighted sequence (PD) or phase-sensitive inversion recovery (PSIR) [15; 21]. STIR seems to be more sensitive than T2-weighted sequences to the detection of lesions but provides more artefacts [30; 31]. PSIR appears to be very sensitive especially in cervical cord, but is currently not available or used in all centers [32].

Using two different planes (i.e. sagittal + axial) is also a way to a greater detection of spinal cord lesions [15; 21]. Galler et al. demonstrated that using combined sagittal and axial scans, compared with sagittal scans alone, improved lesion detection of 22% additional lesions, especially for lesions with small axial

diameters, suggesting including biplanar spinal MR scans as saggital scans underestimate lesions [33]. Different works demonstrate the feasibility of whole spinal cord coverage which would be ideal but currently not performed in clinical practice [8].

Finally, because spinal cord lesions in MS are mostly in the cervical cord, a single sagittal acquisition on the whole cervical level to the upper thoracic spinal cord could be sufficient and improve image quality by a better resolution [15].

In routine

In clinical practice, there were recommendation to perform a spinal cord MRI in the diagnostic workup in any CIS patients suspected of MS not fulfilling McDonald criteria after brain MRI, in patients presenting with spinal cord symptoms (exclusion of a non-demyelinating pathology), in case of patients with an equivocal brain MRI aspect (with vascular risk factors or differential diagnosis), in case of suspicion of primary progressive MS, in case of radiologically isolated syndromes, for its diagnostic value [21].

Currently, as spinal cord MRI provides additional relevant information on the prognosis of the patients, it could be advised to perform a spinal cord MRI systematically at initial work-up in case of suspected or definite MS. However, spinal cord remains not recommended in a systematic MR follow-up, but should be carried out in cases of clinical spinal symptomatology or in case of occurrence of a secondary progressive course.

Conflict of interest

The authors have not declared links of interest in relation to this article.

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