THE „NEW“CLINICALLY ISOLATED SYNDROME (CIS): TO TREAT OR NOT TO TREAT? – NO

K. Vass
Austria

There is no doubt that multiple sclerosis (MS) should be treated early on. Before the establishment of the McDonalds 2010 criteria not all patients requiring treatment met all criteria of MS and had to be labeled as CIS. With the introduction of the new criteria it became possible to diagnose MS in patients presenting with only one clinical episode, leaving the diagnosis of CIS only to those patients who did not meet the criterion of dissemination in space (DIT) and/or the criterion of dissemination in time (DIT) clinically and in the first MRI scan. These patients would either have only one or two lesions in the MRI and/or no contrast enhancement. The open question is whether these patients should be treated with disease modifying therapies. I think they should not be treated. My arguments are:

1) Although with the exception of one study (ETOMS, Comi et al 2001) all the other relevant studies (CHAMPS, Jacobs et al 2000; BENEFIT, Kappos 2006; PRECISE, Comi et al 2009; REFLEX, Comi et al 2012) on treatment of CIS allowed to include patients with as few as 2 lesions on T2 weighted MRI scans, the actual mean lesion load in all studies was as high as 20 to 30 lesions. Thus there is only weak evidence on the effect of disease modifying therapies (DMT) in only mildly affected patients.

2) An abnormal MRI goes along with a likelihood of up to 88% to develop clinically definitive MS (CDMS). Yet within 2 years only 50% of the patients convert to CDMS. In the same study 12% had not even converted after 20 years (Brex et al 2008). Thus CIS patients presenting with an abnormal MRI are likely to develop CDMS, but the time to conversion may be considerably long especially with only a few lesions at baseline.

3) MS might be a disabling disease yet it takes a considerable amount of time until patients acquire significant disability and the worsening is usually preceded by further clinical relapses or at least further activity in the MRI (Confavreux et al 2000). Similarly brain atrophy may develop quit early in the course of the disease, but again the development is only slow (Dalton et al 2002).

4) A final argument against an immediate treatment of patients with “new” CIS comes from the patient’s perspective. Although there are only sparse data available, clinical experience shows that many patients, being usually at an age were most people are just at the beginning of their adult life, having just founded their own families and started their professional carriers being confronted with a possible risk to develop a chronic disease like CDMS, need a considerable amount of time to cope this information. Some of them bluntly refuse to start a therapy for a disease of which they know it may take a considerable amount of time until it actually will develop or which may even never develop. A frequent argument is that the therapies do not cure the threat but may go along with unpleasant though harmless side effects. In addition patients are anxious they will be reminded of having the risk of a severe disease every time when giving themselves the injection. This notion is underlined by a recently published survey with Austrian CIS patients (according to the original definition) where only 54% opted to DMTs within the 24 months after the first neurological episode (Fazekas et al 2010).

In conclusion although MS should be treated already at its earliest stages, there are cases, in particular those who may be labeled as “new” CIS, who should not be forced into a therapy they are not willing to accept. Depending on local regulations and reimbursement issues they should be informed about available treatment options. Yet, I think much more important than treating these usually young patients immediately at the time of their first symptoms is to gain their confidence that they will show up regularly for clinical controls and for repeated MRIs. In case of any indication of new MRI activity or new clinical signs most of them will accept importance to start with a DMT.

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