What to do when confronted by an patient with an radiologically isolated syndrome

Jeremy Chataway, Practical neurology 2010; 10 271-277
Multiple sclerosis is an inflammatory, demyelinating condition of the central nervous system.

Clinically isolated syndrome is an individual's first episode caused by inflammation or demyelination of nerve tissue.

Radiologically isolated syndrome - presence of anomalies, highly suggestive of multiple sclerosis on MRI in the absence of MS symptoms.

Demyelinating Disease Continuum

- Radiologically isolated syndrome
- Clinically isolated syndrome
- Multiple sclerosis
  - RRMS
  - SPMS
  - PPMS
  - PRMS
## McDonald criteria

### McDonald Criteria for MS

<table>
<thead>
<tr>
<th>Attacks</th>
<th>Clinical lesions</th>
<th>Requirements for diagnosis MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 or more</td>
<td>2 or more</td>
<td>None</td>
</tr>
<tr>
<td>2 or more</td>
<td>1 lesion</td>
<td>Dissemination in space demonstrated by MRI (or CSF or await further attack)</td>
</tr>
<tr>
<td>1 attack</td>
<td>2 lesion</td>
<td>Dissemination in time demonstrated by MRI (or second clinical attack)</td>
</tr>
<tr>
<td>1 attack</td>
<td>1 lesion</td>
<td>Dissemination in space and time demonstrated by MRI (or CSF and second attack)</td>
</tr>
<tr>
<td>0 attack</td>
<td>Insidious neurological progression suggestive of MS</td>
<td>2 out of 3 of following: Positive brain MRI Positive spinal cord MRI Positive CSF</td>
</tr>
</tbody>
</table>
The clinically isolated syndrome

- **Dissemination in space:**
  - MRI
  - positive CSF and 2 or more lesions consistent with MS

- **Dissemination in time:**
  - MRI
  - a second clinical attack
Barkhof – Tintore criteria

**MRI criteria for MS**

**Dissemination in Space**

3 out of 4 of the Barkhof criteria:

- 1 Gd-enhancing brain or cord lesion or 9 T2 hyperintense brain and/or cord lesions if there is no Gd-enhancement
- 1 or more brain infratentorial or cord lesion
- 1 or more juxtacortical lesion
- 3 or more periventricular lesions

*Note: Individual cord lesions can contribute along with brain lesions to reach required number of T2 lesions*
Kaplan–Meier estimates of the time from clinically isolated syndrome to clinically definite multiple sclerosis, according to the number of Barkhof–Tintore criteria fulfilled
Radiologically isolated syndrome (RIS)

- More and more patients undergoing MRI for evaluation of head trauma or migraine, are found to have incidental white matter pathology in the CNS that are highly suggestive of demyelinating pathology on the basis of their location and morphology in the CNS.
The groups have generally used the Barkhof–Tintore criteria (?3 positive) as for the clinically isolated syndrome, with no other disease process felt likely and no preceding neurological events.

Four major studies have tackled this issue. Leburn (n= 70) Okuda, (n= 44) Leburn (n= 40) Siva (n= 33)
The Leburn study (n=70); 2000-2008

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
<th>Mean age of presentation</th>
<th>Mean follow up</th>
<th>Female:Male ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache/migrane</td>
<td>30</td>
<td>36 years</td>
<td>5.2 years</td>
<td>3:1</td>
</tr>
<tr>
<td>Migraine</td>
<td>30</td>
<td>36 years</td>
<td>5.2 years</td>
<td>3:1</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radicular pain</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volunteers</td>
<td>3</td>
<td></td>
<td></td>
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</tbody>
</table>

23 (33%) had a clinical conversion to Clinically isolated syndrome at mean time from MRI of 2.3 years:

- 6 motor cord syndrome
- 6 optic neuritis
- 5 brainstem
- 4 sensory symptoms
- 1 cerebellar involvement
- 1 cognitive deterioration
n  The Okuda study (n=44)

- Headache  (n=17)  Mean age  38 years
- Curiosity   (n=4)  Women       41
- Trauma      (n=4)
- galactrrhoea (n=2)
- panic attacks ( n=2)
- low back pain (n=2)

Longitudal follow up was avalible in 30/44, and of those 30 people 10 developed a clinically isolated syndrome or clinically defeniteMS at median 5.5 years.

5 spinal cord involvement
4 optic nerve involvement
1 brainstem event
Leburn (n=30)

- Headache (n=20)
  9 with positive oligoclonal bands

At mean time 2years (1-5 y) 11 patients developed clinical events.
5 optic neuritis
3 brainstem
2 spinal cord
1 cognitive involvement
Siva study (n=22)

- US (n=9), Turkey (n=13)
- Chronic headache 50%
- Other reasons: syncope, health screening

Median follow up 2.5 years (0.5-12.5)
8 developed an inflammatory syndrome at a median of 2 years.
From these four studies about one-third (52/166) went on to develop at least a clinically isolated syndrome after a radiologically isolated syndrome had been identified on MRI, at about 2 years.
**Proposed diagnostic criteria for the radiologically isolated syndrome**

The presence of incidentally identified CNS white matter anomalies meeting the following MRI criteria:

- Ovoid well circumscribed and homogeneous foci with or without involvement of the corpus callosum

- T2 hyperintensities measuring >3 mm and fulfilling Barkhof criteria (at least three out of four) for dissemination in space

- CNS white matter anomalies not consistent with a vascular pattern

- No historical accounts of remitting clinical symptoms consistent with neurological dysfunction

- The MRI anomalies do not account for clinically apparent impairments in social, occupational or generalised areas of functioning

- The MRI anomalies are not due to the direct physiological effects of substances (recreational drug abuse, toxic exposure) or a medical condition

- Exclusion of individuals with MRI phenotypes suggestive of leukoaraiosis or extensive white matter pathology lacking involvement of the corpus callosum

- The CNS MRI anomalies are not better accounted for by another disease
To treat or not?

If the RIS criteria are not met it seems reasonable to put the scan to one side using the phrase “within normal limits”

If the radiologically criteria are met, then in a few years there is a chance, perhaps up to 30% that the clinically isolated syndrome will occur.
In all scenarious remember other diseases have to be ruled out with appropriate inflammatory/vasculitic/infective blood tests.

There is no treatment opportunity for the radiologically isolated syndrome.

The best solution here is probably a careful discussion allied to watchful waiting by yourself to avoid someone else having to navigate this difficult road.