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## Multiple sclerosis in Thailand

Shanop Shuangshoti \*

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*Multiple sclerosis (MS) is rare in Thailand. The first case was recorded in 1970. To the author's knowledge, 67 Thai patients clinically diagnosed as having MS were reported; 3 of them were said to have pathological studies, but the findings were described for only one of them. There was another case diagnosed by 3 neurologists as having MS but pathological examination disclosed meningoencephalitis. The pathogenesis of MS remains unknown although there is evidence to suggest that MS is an autoimmune disease triggered by virus(es). In the Department of Pathology of Chulalongkorn Hospital, 4 patients who were clinically diagnosed to have MS underwent postmortem examination. They were, however, proven to be 2 cases of subacute necrotizing encephalomyelopathy (Leigh's disease), 1 example of meningoencephalitis and neuritis, and 1 instance of periarteritis nodosa. Diagnosis of MS without pathological confirmation may be erroneous, especially in Thailand where the disease is very rare. There are also many diseases that produce diversified neurological symptoms similar to MS.*

**Key words :** *Multiple sclerosis, Autoimmune disease.*

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*Multiple sclerosis* พบน้อยมากในประเทศไทย มีรายงานครั้งแรกเมื่อ พ.ศ. 2513 เท่าที่ทราบถึงขณะนี้มียารายงานว่าพบผู้ป่วยโรคนี้ในประเทศไทย 67 ราย ผู้ป่วย 3 รายกล่าวว่าได้รับการตรวจทางพยาธิวิทยายืนยัน แต่ได้แสดงพยาธิสภาพให้เห็นเพียง 1 ราย ยังมีผู้ป่วยอีก 1 ราย ที่ได้รับการวินิจฉัยจากผู้เชี่ยวชาญทางประสาทวิทยา 3 ท่านว่าเป็น *Multiple sclerosis* แต่จากการตรวจศพพบว่าเป็นการอักเสบของเยื่อหุ้มสมองและไขสันหลัง พยาธิกำเนิดของ *Multiple sclerosis* ยังไม่เป็นที่ทราบแน่ชัด มีหลักฐานสนับสนุนว่าอาจเป็นโรคทาง *autoimmune* ที่เกี่ยวข้องกับไวรัสที่ภาควิชาพยาธิวิทยา โรงพยาบาลจุฬาลงกรณ์ ได้ทำการตรวจศพผู้ป่วยที่ได้รับการวินิจฉัยทางคลินิกว่าเป็น *Multiple sclerosis* 4 ราย ผลการตรวจทางพยาธิวิทยาพบว่าเป็น *necrotizing encephalomyelopathy* รองเฉียบพลัน (โรคของ Leigh) 2 ราย, การอักเสบของสมอง, เยื่อหุ้มสมอง, ไขสันหลัง, และเส้นประสาท 1 ราย และ *periarthritis nodosa* 1 ราย การวินิจฉัย *Multiple sclerosis* โดยที่ไม่มีการตรวจทางพยาธิวิทยานั้นมีโอกาสผิดพลาดได้มาก โดยเฉพาะในประเทศไทยซึ่งมีอุบัติการณ์ของโรคนี้ต่ำมากเป็นที่น่าสงสัยว่าคนไข้ที่ได้รับการวินิจฉัยทางคลินิกว่าเป็น *Multiple sclerosis* โดยที่ไม่มีการตรวจทางพยาธิวิทยายืนยันนั้นจะเป็น *Multiple sclerosis* จริงสักกี่ราย การที่จะวินิจฉัย *Multiple sclerosis* ในประเทศไทยนั้นคงจะต้องพิจารณาให้รอบคอบ และจะต้องแยกโรคอื่น ๆ ที่ให้อาการและอาการแสดงทางคลินิกที่คล้ายหรือเหมือนกับ *Multiple sclerosis* ออกไปเสียก่อน

Multiple sclerosis (MS) is a demyelinating disease which is exorbitantly uncommon in Thailand. The first autopsy-proven case was reported in 1970.<sup>(1)</sup> Diagnosis of MS without pathological confirmation may be incorrect because there are many other diseases that can give clinical manifestations imitating MS.

### **Pathogenesis of Multiple Sclerosis**

The pathogenesis of MS remains poorly understood in spite of intensive research. However, T cell-mediated autoimmune reaction is thought to be related to MS.<sup>(2)</sup> In this theory, there must be the antigen(s) recognized by macrophages or astrocytes which have major histocompatibility complex class II molecules and act as antigen presenting cells. T-cell receptors respond to the antigen resulting in stimulation of helper T-cells, and subsequent cytokine secretion, T-cell proliferation, and B-cell and macrophage activation. These cells break down the blood-brain barrier and cause wide spread death of oligodendrocytes as well as demyelination.<sup>(2)</sup>

What is(are) the antigen(s) that trigger(s) the autoimmune response? Virus such as canine distemper virus, measles-like morbillivirus in dogs<sup>(3,4)</sup> and human herpesvirus type 6<sup>(5)</sup> are suspected to cause MS. But despite many claims, virus has not yet been isolated from MS patients.<sup>(6)</sup>

Although the autoimmune hypothesis seems to be a reasonable cause for MS, other possible causes must be also looked for. Many patients suffered from receiving immunosuppressive agents due to this hypothesis.<sup>(7)</sup>

### **Diagnostic Criteria and Diagnosis Categories for Multiple Sclerosis<sup>(6)</sup> see appendix.**

According to the criteria, there are many diseases to be excluded before making a diagnosis of MS. Vajjajiva reported a patient with SLE who had clinical presentations resembling MS.<sup>(8)</sup> Although there are numerous investigations for MS such as CSF analysis for oligoclonal band, visual evoked potential, computed tomography and MRI, none is specific.<sup>(9,10)</sup>

### **Pathology of Multiple Sclerosis**

**Macroscopic pathology.** The main pathologic feature of MS is multiple plaques which correspond to demyelinating foci. Hence, plaques are found mainly in the white matter. Plaque is hard. This disease, thus, is called multiple or disseminated sclerosis.<sup>(11)</sup> Early plaque is pink and its color will change to gray when it get older.<sup>(12)</sup> The common locations of plaques are periventricular white matter, the periaqueductal region, the subcortical junction, the optic nerve, chiasm, and tract; brain stem, and spinal cord.<sup>(12)</sup> MS does not involve the peripheral nervous system.<sup>(11)</sup>

**Microscopic pathology.** In acute MS, there is perivascular infiltration of lymphocytes, especially T-cells, and plasma cells.<sup>(13)</sup> Later, demyelination occurs which leads to oligodendroglial proliferation. Astrocytes are reactive and hypertrophic.<sup>(14)</sup> Myelin debris is scavenged by microglia (scavenger cells).<sup>(13,14)</sup>

When the disease becomes chronic there is complete demyelination. Oligodendroglia and perivascular infiltrates disappear. The lesion, then, is replaced by gliosis. <sup>(6,13,14)</sup>

### Data Relating to Multiple Sclerosis in Thailand

To the author's knowledge, 67 patients with MS have been reported. <sup>(10,15)</sup> One series consisted of pediatric patients from 2 to 14 years old with an average age of 8 years. <sup>(10)</sup> The ratio of women to men was 3 to 1. All cases were diagnosed by Posers criteria without pathological examination. <sup>(16)</sup> The other series recorded 50 patients having MS. <sup>(15)</sup> The age ranged from 13-68 years with the mean age of 30.4 years. The female-male proportion was 4 to 1. Three of the cases had pathological studies but the findings were exhibited in only one case. <sup>(1)</sup> There was also another case diagnosed by 3 neurologists as being MS but a pathological examination disclosed meningoencephalitis. <sup>(1)</sup> The author, moreover, had personally contacted with Professor Dr Tavipan Tantachamroon of the Department of Pathology, Faculty of Medicine, Chiang Mai University; Professor Dr Rangsan Panyathanya of the Department of Pathology, Faculty of Medicine and Siriraj Hospital, Mahidol University; and Associate Professor Dr Winyu Mitarnun of the Department of Pathology, Faculty of Medicine, Prince of Songkhla University about their experience upon MS in their institutions. All of them who have been in the field of pathology for more than 25 years stated that there have been no pathologically proven case of MS reported from

their places.

In the Department of Pathology of Chulalongkorn Hospital, 4 patients clinically diagnosed as having MS underwent postmortem examination. However, they were proven to be 2 instances of subacute necrotizing encephalomyelopathy (Leigh's disease), <sup>(17)</sup> 1 example of meningoencephalitis and neuritis, <sup>(18)</sup> and 1 case of periarteritis nodosa. <sup>(19)</sup> The author was informed of the last case by the pathologist who performed the autopsy and he reported that the patient was clinically diagnosed to have had MS.

According to the data, diagnosis of MS without pathological examination may be erroneous, especially in Thailand where this malady is extremely rare. There are many diseases which may give neurological symptoms similar to MS which must first be ruled out.

## Appendix

### Diagnostic Criteria <sup>(6)</sup>

1. Examination must reveal objective abnormalities of the CNS.
2. Involvement must predominantly reflect disease of white matter of long tracts usually comprising:
  - a) pyramidal pathway
  - b) cerebellar pathway
  - c) medial longitudinal fasciculus
  - d) optic nerve
  - e) posterior columns of the spinal cord.
3. Examination or history must implicate affection of two or more areas of the CNS.
  - a) MRI may be used in patients below

the age of 40 to document a second lesion when only one site of abnormality has been demonstrated on examination. A confirmatory MRI must have either four lesions involving the white matter, or three lesions if one is periventricular by location. Acceptable lesions must be greater than 3 mm across.

b) Evoked response testing may be used to document a second lesion.

4. The clinical pattern must consist of

a) two or more separate episodes of worsening involving different sites of the CNS, each lasting at least 24 hours and occurring at least 1 month apart or

b) gradual or step-wise progress over at least 6 months if accompanied by increased CSF IgG synthesis or two or more oligoclonal bands.

5. Age of onset is between 15 and 60 years old.

6. The patient's neurologic condition could not be better attributed to another disease. Laboratory testing that may be advisable in specific cases includes:

- a) CSF analysis
- b) MRI of the head or spine
- c) serum B<sub>12</sub>
- d) human T cell lymphotropic virus type

I titer

- e) sedimentation rate
- f) rheumatoid factor, antinuclear, anti-

DNA antibodies (systemis lupus erythematosus or SLE)

- g) serum VDRL

h) angiotensin-converting enzyme (sarcoidosis)

i) Borrelia serology (Lyme disease)

j) very long chain fatty acids (adrenoleukodystrophy)

k) serum or CSF lactate, muscle biopsy, or mitochondrial DNA analysis.

### Diagnostic Categories <sup>(6)</sup>

1. Definite MS: all six criteria fulfilled.

2. Probable MS: all six criteria fulfilled except (a) only one objective abnormality despite two symptomatic episodes or (b) one symptomatic episode and unrelated signs detected on examination.

3. At risk for MS: all six criteria fulfilled except one symptomatic episode and corresponding signs detected on examination.

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