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Corrigendum to 'Multiple sclerosis: New insights and trends'

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ABSTRACT

Keywords:

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Multiple sclerosis (MS) is the most famous autoimmune disease attacking the central nervous system. It attacks people from age 20–50 years old and the females' attacks double than males' attacks. MS is an autoimmune disease affecting principally the central nervous system that causes nerve sheath demyelination, followed by axon damage and paralysis. MS symptoms include muscle weakness, weak reflexes, muscle spasm, difficulties in movement and unbalance. Many factors may be responsible for MS: micro-organism, virus, smoking, stress, environmental toxins, contaminated diet and gout. MS is widely spread in the population in North Europe and this is related to lack of vitamin D due to decrease of sunlight exposure. MS biomarkers include nitric oxide, interleukin-6, nitric oxide synthase, fetuin-A and osteopontin. MS is not a genetic disease (not transferred from parents into next generations) but MS appears when leukocyte antigen system-related genes are changed in human chromosome 6. The physiology of MS patients is controlled by numbers of biological processes such as activation of immune-inflammatory, oxidative and nitrosative stress pathways. MS includes two main steps: (1) myelin sheath destruction and formation of lesions and, (2) inflammation. Four types of MS can be distinguished: relapsing-remitting, primary progressive, secondary progressive and progressive relapsing. Nine treatments have been accepted for relapsing-remitting MS type: interferon β -1a, interferon β -1b, mitoxantrone, natalizumab, glatiramer acetate, fingolimod, dimethyl fumarate, teriflunomide, and alemtuzumab. However, the only treatment used is mitoxantrone for progressive MS with many side effects. Complementary treatments are also used in MS treatments such as vitamin D, Yoga, medicinal plants, oxygen therapy, acupuncture and reflexology.

1. Introduction

Scientist Jean-Martin Charcot was the first one who had discovered the disease in 1868 [1]. It is the most famous and pronounced autoimmune disease that attacks the central nervous system [2]. According to World Health Organization reports in 2008, 2–2.5 million with multiple sclerosis (MS) disease were recorded in the world [3], and approximately 20000 MS patients died all over the world in 2012, comparing to 12000 deaths in 1990 [4]. MS attacks people from age 20–

50 years old and the records shows that females' attacks are double than males' attacks [5,6]. Disseminated sclerosis and encephalomyelitis disseminate are two alternative names of MS. MS is an autoimmune disease induced by external and environmental factors that initiate genetic changes such as virus-induced immune disturbances [7]. There are many types of MS, sometimes occurring in isolated neuron (relapsing type) or spreading to few or many neurons (progressive type) [8]. The MS characteristic features are common disability, moving limits, low personal activity-related self-effectiveness, limitation of self-regulatory concepts, sociodemographic factors restrictions, declined employment state, and decreased educational level [9]. The MS symptoms may disappear completely, however, the permanent neurological problems happen when the disease advances [8]. MS symptoms occur when the nerve cells myelin sheath in the central nervous system (brain and spinal cord) start to be injured and consequently damaged. MS is associated with many symptoms and these include: physical, mental, and sometimes psychiatric disturbances [10–12], due to the neural

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damage which blocks the communication among different parts of the nervous system.

The mechanism responsible for occurrence of MS can be summarized into two reasons: (1) destruction of the myelin sheath by the immune system, and (2) failure of the myelin-producing cells to produce new sheathes [13]. The two above mentioned reasons include numerous genetic and environmental factors *e.g.* heredity, pollution, microbial and viral infections [11,14,15]. MS is diagnosed depending on the patient status and the medical check-up investigations.

Recovery from organ-specific autoimmune diseases in early phases relies on mobilization of endogenous repair mechanisms and local factors that control them. The natural killer (NK) cells are quickly moved to the organs aimed by autoimmunity and the number of NK cells are increased when inflammatory case occurs. The NK cells are recalled in the brain subventricular zone in the progressive type of MS in both human and animal models. These NK cells are established very close to subventricular zone neural stem cells (NSCs), consequently the cells begin to secrete interleukin-15 and maintain the NK cells function. Furthermore, the NK cells decrease the functional capability of NSCs following MS inflammation, so neuro repair is found due to communication of both NK and NSCs cells [16]. Different types of disability (unmovable) of the upper limb can be found in MS incidence and a training program is proposed and directed toward the upper limbs to improve the limb function and structure in MS but it has no observable effect on the upper limb capability and performance in MS patients with advanced types [17].

All the MS treatments try to improve the neuronal function following MS occurrence and stop the progress of the disease [11]. The use of treatments in MS can induce adverse side effects. The long-term treatments with good results are observed in MS teenager women with relapsing type that have few neurons damaged [18]. MS decreases life span with an average of 5–10 years than other healthy ones [10,19]. Many treatments and diagnostic procedures of MS are in the process of development.

2. MS symptoms

MS is an autoimmune disease affecting principally the central nervous system (brain and spinal cord) that cause nerve sheath demyelination followed by axon damage and consequently paralysis [20]. Many distinguished lesions are found in the lower urinary tract as pronounced symptoms in MS patients [21]. On the other hand, MS is a major reason for human disability of neurological origin in the young adults where depression is the most observed psychiatric disorder [22]. Central and peripheral auditory disturbances always appear in MS [23]. On the other hand, the typical optic neuritis is usually the presenting symptom of MS [24]. Sleep disorder, exhaustion, and pain are other symptoms associated with MS [25].

MS symptoms depend on the specific nerve attack in the central nervous system and may finally lead to loss of sensitivity in sensation such as muscle weakness, weak reflexes, muscle spasm, difficulties in movement; problems in coordination and balance; problem in speech, optic problem, tired feeling, acute or chronic pain, and bladder and bowel difficulties. Depression is always associated with MS due to variable mood of MS patients. In addition, thinking and emotional problems are also observed in MS. There are many factors that increase MS disease symptoms *e.g.* viral infections such as cold, influenza, and gastrointestinal problems. Females are more sensitive to MS

than males especially during the first three months after baby birth. Other factors do not play a role in MS reappearance such as vaccination, breast feeding, and physical status [10,25,26]. The expanded disability status scale (EDSS) is a well-known test of MS-associated disability, in addition to other clinical investigations [27,28]. Stress is also a main cause of MS [29]. Figure 1 reveals MS main symptoms [30].

3. MS causes

Up to date, the reasons for MS incidence have not been found. However, a combination of external and environmental factors that initiate genetic changes include pollution, stress as well as viral and bacterial infections. These factors can be summarized into: microbial, viral and other infections.

3.1. Microbial infection

The infection with microbes has been associated in the main processes of introducing and increasing the incidence of MS [31]. MS can be induced by many microbes [11], and moving from one place to another increases microbial infection to induce MS [14,15].

The infectious disease, paratuberculosis, mainly affects wild and domestic ruminants. This disease is induced by *Mycobacterium avium paratuberculosis* (MAP), where MAP correlated to MS incidence. The MAP DNA was found in 4/7 (57.14%) goats, and in 14/25 (56%) sheep cheese using qPCR. In goat, MAP produced type S strain of MAP, and this MAP occurred in quantities ranging from 1.8×10^4 to 6×10^4 MAP cells/g of cheese. In this study, 56.57% and 66.60% of cheese tested showed positive results for MAP and these can lead to increased incidence of MS in human [32].

The mechanisms of MS induction include hygiene hypothesis and prevalence hypothesis. The hygiene hypothesis assumes that microbial infection occurs in early life but human can be

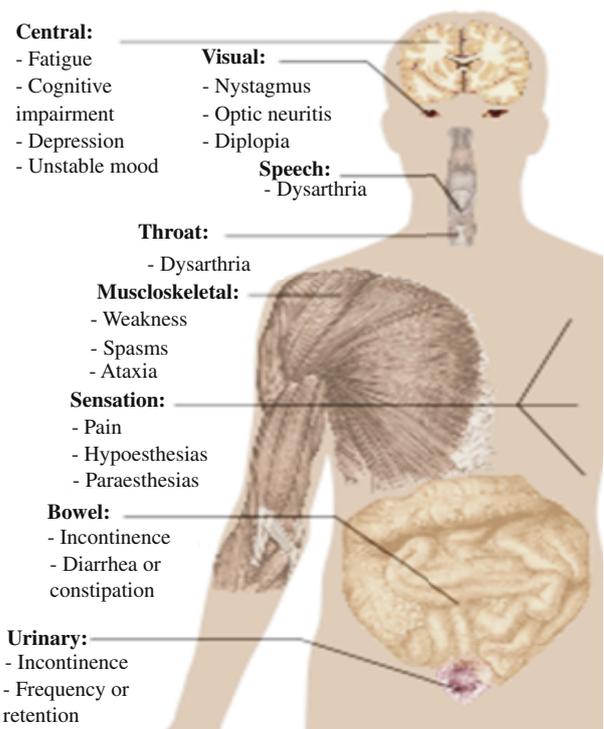


Figure 1. MS main symptoms [30]. https://en.m.wikipedia.org/wiki/Multiple_sclerosis.

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