PARKINSON'S DISEASE

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28/06/2013

Parkinson's disease (PD) is the second most common neurodegenerative disorder in Australia, with approximately 25 new cases of this disease being diagnosed every day. The major pathological feature of PD is a loss of neurons in a region of the brain termed the substantia nigra. These neurons produce the neurotransmitter dopamine which is important for coordination of movement. PD is a chronic and incurable condition that progressively worsens over time leading to significantly disabling motor symptoms, which reduce the patient's quality of life (1).

Symptoms and their impact on quality of life

The cardinal symptoms of PD include resting tremor, slowness of movement, muscle rigidity and postural instability. Tremor is the most common and generally the first symptom to develop which regularly affects the hands but can also include the legs, lips, chin and jaw (2). Slowness of movement involves difficulty with planning, initiating and executing movement whereas muscle rigidity refers to increased resistance of muscle during passive movements of patients limbs (2). Postural instability is rarely apparent at the initial presentation, however, it can cause significant health problems as it is the primary cause of falls associated with PD. Remarkably, these symptoms appear only when 50-70% of dopaminergic neurons in the substantia nigra are lost, therefore at the time the patient is diagnosed with PD, dopamine levels in the substantia nigra are very low. Hence, there is an urgent need for early biomarkers of the disease in order to diagnose the disease in its early stage before the motor symptoms become evident.

It is important to recognise that in addition to movement disturbances, PD patients suffer from many non-motor symptoms such as altered smell, taste, vision, cardiovascular function, sleep, gastric and bowel function, mood, and cognition (3). Retrospective studies showed that some non-motor symptoms can appear several years before the onset of the classical motor symptoms. Many of these symptoms tend to accumulate in PD patients and increase in severity with progression of the disease. In fact, PD patients reported that the non-motor symptoms may even have a greater negative impact on their quality of life than the motor impairments and motor complications (4).

Genetic and environmental factors contributing to PD

Although PD was first described in "An Essay on the Shaking Palsy" by James Parkinson in 1817, the aetiology of PD remains unknown. There is increasing evidence to support the 'multi-hit' hypothesis encompassing both environmental and genetic factors. In 90-95% of PD cases there is no apparent genetic linkage, these cases are referred to as idiopathic or sporadic PD, the remaining 5-10% of patients have the inherited form of the disease (5).

Epidemiological studies have found an association with residing rurally and exposure to certain herbicides and pesticides such as rotenone with an increased risk of developing PD later in life (6). Another factor that has been shown to directly relate to the onset of PD is the aging process. The specific influence of aging on pathophysiology is not known, however it is predicted to

contribute by the older dopaminergic neurons having a heightened vulnerability to toxic insult from increasing failure of normal cellular physiological and biochemical processes (7).

Inflammation is now thought to play a role in the pathogenesis of PD. Chronic inflammatory diseases and disorders that result in peripheral inflammation appear to influence the pathogenesis and progression of PD, with evidence suggesting a link between peripheral inflammation and PD (8). The evidence of neuroinflammation's potential role in PD has led to numerous studies which have assessed non-steroidal anti-inflammatory drugs (NSAIDs) influence on the incidence of PD and their possible uses as a protective therapy (9). A large study of more than 80,000 men and 90,000 women reported the risk of PD was lower among ibuprofen users, however no associations were seen with other NSAIDs such as aspirin (10). Despite this finding, some studies have failed to detect protective effects associated with the consumption of NSAIDs. Also, the long term use of this drug class is linked to serious gastrointestinal effects as well as other side effects, therefore further more conclusive studies need to be conducted to establish if there is a role for NSAIDS in PD therapy (9).

Diagnosis

It is difficult to diagnose PD as diagnosis is primarily based on the symptoms and physical examination and there is no laboratory test available today to confirm the diagnosis. Several clinical, laboratory, and imaging tests are now being investigated as potential early markers of Parkinson's disease (11).

Various non-motor signs (such as olfactory dysfunction, sleep disturbances and constipation) have been suggested as early biomarkers that precede the typical motor symptoms in PD. Functional neuroimaging has advanced over the last few years and led to novel diagnostic methods such as magnetic resonance imaging. Multiple biochemical markers present in cerebrospinal fluid and blood of PD patients have also been developed and tested. None of these are yet established as PD biomarkers, thus the search for effective biomarkers continues. It is most likely, however, that a combination of biomarkers that comprise different features of the disease (clinical, biochemical, genetic and imaging data) may be required for this complex disorder (11) .

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