

## Chemokines and Cytokines to the Rescue to Distinguish Lyme Neuroborreliosis Manifesting Alzheimer's Symptoms from Alzheimer's Disease which is Especially Important in Areas Endemic for Tick Borne Diseases

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"It is important for Neurologists to be able to distinguish Alzheimer's Disease, from Lyme Neuroborreliosis, manifesting Alzheimer's Symptoms as this latter illness can be treated with antibiotics in the early stages".

It has been stated, "Like its close spirochetal cousin *Treponema pallidum, Borrelia burgdorferi* can cause disabling neurological manifestations and present a puzzling diagnostic challenge" [1].

Coyle noted that in Lyme disease, "neurological involvement occurs in up to 40% of symptomatic infections and includes both CNS and PNS involvement" [2]. The literature also notes that Lyme Neuroborreliosis has been misdiagnosed for Alzheimer's Disease as was seen in the case of country and western singer Mr Kris Kristofferson [3].

Kristoferitsch., *et al.* discussed the presence of dementia-like syndromes associated with Lyme borreliosis [4]. These investigators further stated that that *Borrelia burgdorferi* could cause or even trigger primary dementia such as Alzheimer's Disease [4]. This investigation also noted that there occurred "Gait disturbances early in the disease course" as a characteristic feature [4].

Kristoferitsch., *et al.* found that "the response to 2 - 4 weeks of antibiotic treatment with ceftriaxone was excellent" [4]. Kristoferitsch., *et al.* have noted that it is crucial to be aware of the possibility of the occurrence of Lyme Neuroborreliosis because early antibiotic treatment will prevent "permanent sequelae that may occur throughout the further course of the untreated disease" [4].

Miklossy, et al. investigated patients with concurrent Alzheimer's Disease and Lyme Neuroborreliosis, and found that "the recovery of cognitive decline in the patient with Lyme disease and AD-type dementia (Alzheimer's Disease type) following antibiotic treatment suggests that in an analogous way to *Treponema pallidum, Borrelia burgdorferi* can cause dementia which may be prevented or slow down by antibiotic treatment" [5].

Correa., et al. noted the importance of the presence of chemokines "in the early stages of Alzheimer's Disease" [6]. This investigation studied "levels of beta-amyloid, tau, phospho-tau and chemokines (CCL2, CXCL8, and CXCL10) in the CSF in patients with Alzheimer's Disease and healthy controls" [6]. These investigators found that levels of p-tau were higher in Alzheimer's Disease patients when compared with the healthy control group, and this was contrasted with the fact that the tau/p-tau ratio was decreased [6]. The expression of

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the chemokine CCL2 was found to increase in patients with Alzheimer's Disease. In addition there was a "positive correlation between the beta amyloid levels and all of the chemokines investigated in this study" [6]. A positive correlation also was found between the CCL2 and p-tau levels [6]. An important finding in this investigation was that "the levels of the CCL2 present in the CSF were involved in the pathogenesis of Alzheimer's disease". This study also proposed that the CCL2 could be an additional and useful marker in the monitoring of Alzheimer's disease progression [6].

Pietikainen., *et al.* noted that currently a diagnosis of Lyme Neuroborreliosis is based upon "intrathecal production of antibodies" [7]. These investigators point out that a new and promising means of investigating the presence of Lyme Neuroborreliosis involves the presence of the cytokine CXCL13 and its measurement [7]. Patients with Lyme Neuroborreliosis and Neurosyphilis (tertiary syphilis is rarely seen in the 21<sup>st</sup> century) showed significantly higher levels of CXCL13 in their CSF [3,7]. These investigators further stated that, "Chemokine CXCL13 is at the present time, the best biomarker for Lyme Neuroborreliosis" [7].

Lepenta., et al. have stated that, "Borrelia species are able to invade the brain and remain there for years, subsequently causing dementia; state that an undetermined number of patients with Alzheimer's Disease have late tertiary neuroborreliosis" [8].

An extremely important point put forth as relates to the findings of the investigation of Lepenta., et al. vis a vis Lyme Neuroborreliosis was, "no patient showed the classic marker of the disease that is the Chronic Erythema Migrans (ECM) and only 3 had arthritis, which is the other clinical marker of this pathology" [8]. These investigators thus put forth the conclusion, "that Lyme disease can present as pure neurological forms, without extra neural findings" [8].

Lepenta., et al. further stated that "The World Health Organization in the update of the ICD-11 year 2018 (International Classification of Diseases) included the codes for Lyme Borreliosis related to this research "Lyme neuroborreliosis", "dementia due to Lyme disease" and "central nervous system demyelization due to Lyme borreliosis" [8].

It is important for Neurologists to be able to distinguish Alzheimer's Disease, from Lyme Neuroborreliosis, manifesting Alzheimer's Symptoms [4-8]. Lyme Neuroborreliosis can be treated with antibiotics in the early stages [4-8].

Chemokines and Cytokines thus can play a useful diagnostic role in distinguishing Alzheimer's Disease from Lyme Neuroborreliosis manifesting Alzheimer's Symptoms. This fact is especially important in Tick Borne Disease Endemic Areas!!

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