DEFICIENCIES IN COMPLEMENT SYSTEM

Complement system is made up of a regulated network of proteins that are involved in inflammation, opsonization and phagocytosis. But the uncontrolled activity of the complement can lead to many autoimmune diseases.

Brain cells are specially susceptible to complement system because they are exposed, not only to the circulating factors but also to locally synthesized complement proteins. The activation and massive release of complement factors can be dangerous to brain cells but, conversely, it can also have an important paper in normal development and protection of the brain. A case of the presence of both effects is Alzheimer Disease (AD) (Kolev MV, et al, Curr Neuropharmacol 2009).

In AD, different patterns of expression during the different stages of the disease have been noticed, and have also been related with the deposition and maturation of β-Amyloid plaques. This disease is an example of how lack of regulation can lead to autodestruction of the cells.

Regarding to the protective paper of complement, it has been found that C1q, C3 and C4d factors increase during the early stages of AD. This fact is positively correlated with the removal of Aβ plaques from the nervous tissue. C1q induces the expression of genes that are neuroprotective, while C3 may act as a chemoattractant factor for microglial cells involved in the clearance of Aβ protein deposits, mantaining tissue homeostasis (Kolev MV, et al, Curr Neuropharmacol 2009).

The problem in nervous tissue is that neurons poorly express complement regulators, what makes this tissue even more susceptible to complement-mediated death. Aβ plaques can produce cell lysis, which would activate the complement, increasing the concentration of its factors. But this is not accompanied by an increasement of complement regulators, and so this lead to an overreaction, huge inflammation and tissue damage (Orsini F, et al, Front Cell Neurosci 2014).

Moreover, terminal products of both classical and alternative pathway (C9, C5b9, C5) have been found to be toxic for the neurons, showing detrimental effects during the pathological progression of AD and accumulation in the latest stages of the disease.

When the complement system turns completely uncontrolled, the overexpression of its factors also leads to a block of the synaptic elements due to the anchoring of C3 factor to the neurons, when trying to help to eliminate plaques.

Systemic lupus erythematosus (SLE), also known simply as lupus, is an autoimmune disease in which the body's immune system mistakenly attacks healthy tissue in many parts of the body.

Common symptoms include painful and swollen joints, fever, chest pain, hair loss, mouth ulcers, swollen lymph nodes, feeling tired, and a red rash which is most commonly on the face. One manifestation of SLE is abnormalities in apoptosis. In SLE, the body's immune system produces antibodies against itself.

Some cases of Systemic Lupus Erythematosus (SLE) have been found in patients with deficiencies in some of the complement components. Many studies have been carried out to analyze these cases in order to obtain some conclusions.

Research indicates SLE may have a genetic link. SLE does run in families, but no single causal gene has been

identified. An analysis was made to report the genetic basis of C7 deficiency. The results provided more evidence that the molecular bases for complement component C7 deficiency are heterogeneous, because different individuals carry distinct molecular defects (Barroso S, et al, Immunology. July 2006).

Another study was also carried out to obtain the frequency of hereditary complete complement deficiencies among families with two or more SLE patients by measuring the total complement hemolytic activity or CH50, and it was found that even among families with multiple SLE patients, monogenetic forms of the disease caused by loss of function mutations in complement components are highly unusual (Aggarwal R, et al, Lupus. 2010 January).

It can only be concluded that SLE is presumably caused by an unknown environmental trigger, acting on persons with genetic susceptibility and defects in the immune system.

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