Are Mast Cells the Key to Multiple Sclerosis?

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Mast cells are not present in the normal and unaffected human brain [1], but were observed in the brains of MS patient 1890 [2]. From recent observations, it seems that all symptoms we recognize in MS may be explained by the presence of these cells.

The numbers of mast cells in the plaque border zones of females is twice as high as in males [3]. This fact may explain why MS is more abundant in females than men [4].

Stimulated mast cells secrete histamine, and histamine evokes oedema formation which is frequently registered in MS.

Stimulated mast cells even secrete proteases. Mast cell proteases dissolves myelin [5], and demyelination is of course the most serious and MS-defining effect of the mast cells. A strong association between mast cells and MS is further strengthened by the fact that elevated mast cell tryptase is observed in the cerebrospinal fluid of MS patients [6], as well as the observation that mast cell transcripts are increased within and outside multiple sclerosis lesions [7].

Mast cells recover after depletion of their granular contents (e.g., histamine and protease) [8] which may explain the relapsing remitting periods that often characterize the disease; Massive stimulation of the mast cells (relapsing), and then the silent period (remitting) when the cells recover and build up capacity for another relapse.

The theory that mast cells influence the development of MS is fascinating close and simple to follow, and all the more should, at least from a theoretical point of view, be easy to challenge since we have mast cell blockers, and also antihistamines that may block the histamine opening up of BB-barrier, and thus hopefully stop secretagoques, what ever they are, to stimulate the perivascular mast cells.

One may argue that what we observe is not “the hen, but the hen’s egg;” just some reaction to the primary cause ending up to MS. If the mast cell is the primary cause, however, we may have some fascinating perspectives for the cure of MS.

It has been argued, based on former publications on mast cells and MS [9-11], that their numbers are far to low to be of any significance. Many former studies on mast cells in autopsy materials are, however, based on uncertain staining methods [12]. Recent observations demonstrate that the numbers of mast cells/area in border zones of MS-plaques is 10 times higher than former registered [3], which makes it highly probable that mast cells may have an effective biological influence. In addition they are clustered along venules in a way that may explain the oedema formations observed in MS [13].

What may stimulate the mast cells we don't know. It has long been speculations on the various milieu- and eventually cultural factors as the basis for the geographically uneven distribution of MS. This has been evaluated as genetic variations between populations. It is, however, closer at hands to point to nutritional variations, which in itself may explain why MS in Norway earlier on was a typical inland phenomenon, and now the last 50-70 years just as common in the coastal areas [14].

It seems that behaviour and “Way of life” may be important as well. We know that mast cells may be stimulated by long lasting and acute mental stress [15,16], and the association to our neuro-endocrine system has been forwarded. It has even been demonstrated that our neuro-endocrine system secretes protein that stimulates mast cells [17], which strongly indicates a relation between behaviour, stress and MS.

The initial invasion of mast cells into the brain is probably the result of a more general invasive reaction due to a childhood infection [18,19], and may even perhaps indicate a possible protective role for the mast cells against immune reactions? [20] This potentially protective role of mast cells in MS is, however, contradicted by observations that the histamine-antagonist hydroxyzine, which blocks the effects of histamine on blood vessels and also partly blocks mast cells in the brain, has the potential of reducing MS-symptoms in both women and men [21].

Our neurologic institutions priority of studying genetics and MS is based on the assumption that MS is an autoimmune and genetic determined disease. It is hard to understand such priority, although of course interesting in itself, although of no practical consequences for any actual MS-patient. It seems to be straight forward arguments for assuming MS to be a genetic based disease, like studies on siblings, families, races etc. However, consequences of epigenetic heritage from grand- and grand-grand-parents nutritional and behavioural habits may be more likely one of the candidates for inducing of MS than "regular" genetic heritage (Figure 1).

References

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Received May 23, 2015; Accepted July 10, 2015; Published July 17, 2015

Citation: Kruger PG (2015) Are Mast Cells the Key to Multiple Sclerosis? J Mult Scler (Foster City) 2:146. doi:10.4172/2376-0389.1000146

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