TITLE: PARTICIPATION OF AUTOPHAGY IN THE ELDERLY WITH MULTIBACILLARY LEPROSY

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ABSTRACT:

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, an obligate intracellular bacterium that affects macrophages in the skin and Schwan cells in the peripheral nerves. The disease shows a spectrum of clinical forms, as determined by the bacillary load and by the host's ability to mount its immune response to the pathogen. Such spectrum ranges from tuberculoid or paucibacillary forms (PB) to lepromatous or multibacillary (MB) and intermediate. Prior study performed by our group demonstrated positive regulation -through high level of LC3-II expression -, thus characterizing increased formation of autophagosome in young adult PB patients, while, in MB, such relation was negative. The association between leprosy, ageing and autophagy, that still lacks clarification, was the purpose of this work. The expression of BCL2 gene was analyzed by RT-qPCR in cutaneous fragments from 12 MB patients. This gene encodes the protein Bcl-2 in charge of regulating autophagy through interaction with initiator proteins of this process, such as beclin-1 encoded by the gene BECN1, that plays a critical role in autophagic programmed cell death. We noted an increased gene expression in elderly patients, in comparison with younger ones, which suggests a reduction in the autophagic mechanism in seniors. Higher expression of BCL-2 may possibly inhibit beclin-1 and influence crucial steps in autophagic pathways, since the formation of phagophores up to the maturity of autophagosome. In addition, the expression of LC3, the major protein marker of autophagy, was analyzed by Western Blot in proteins obtained in trizol through dialysis process in 10 PB and MB patients. The reduction of LC3I and II in elderly PB and MB patients suggests lower formation of autophagosomes within the age range (≥ 60 years). Such data suggest a negative regulation of autophagic flow in elderly patients, when compared to younger, thus possibly influencing leprosy polarization. Taken together, our results corroborate the phenomenon of age-related changes in the immune system.

KEYWORDS: Leprosy, autophagy, ageing.

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