Minocycline inhibits the growth of glioma through endoplasmic reticulum stress-induced autophagic cell death and caspase activation

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Abstract

Minocycline, a second-generation tetracycline, has marked neuroprotective properties in various models of neurological diseases. Besides neuroprotection, minocycline has the capability of tumor inhibition. Here we demonstrated that minocycline induced glioma cell death through induction of both autophagy and apoptosis. Minocycline induced autophagy was confirmed by acridine orange and the conversion of cytosolic LC3-I to autophagosome membrane-bound LC3-II. Pretreatment with autophagy inhibitor 3-methyladenine (3-MA) suppressed the induction of acidic vesicular organelles and the accumulation of LC3-II in glioma cells treated with minocycline. However, minocycline still induced cell death resulting from the activation of caspase-3. The combined pretreatment with 3-MA and caspase inhibitor (Z-VAD) in glioma cells resulted in a reduction of cell cytotoxicity. Moreover, we found that minocycline treatment also induced eIF2α phosphorylation and thereby the activation an endoplasmic reticulum (ER) stress that signified the onset of autophagy and apoptosis. These findings suggest that minocycline induced glioma cell death through ER stress mediated autophagy and apoptosis.