Supperession of Choroidal Neovascularization by Adeno-associated Virus Vector Expressing Angiostatin

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摘要

Abstract

PURPOSE: To test the efficacy of a recombinant adeno-associated virus (rAAV) vector that expresses mouse angiostatin in suppressing experimental choroidal neovascularization (CNV) in a rat model. METHODS: An rAAV vector, rAAV-angiostatin, was constructed to deliver the mouse angiostatin gene. rAAV-angiostatin and a control virus, rAAV-lacZ, were delivered in vivo by subretinal injection in Brown Norway rats, and the delivery was confirmed by reverse-transcriptase polymerase chain reaction (RT-PCR). For a CNV suppression experiment, CNV was generated by fundus krypton laser photocoagulation 7 days after the viral vector injection and was evaluated by fluorescein angiography (FA) and histology. Apoptosis in retina was analyzed using the TUNEL assay. Inflammation in the retina was investigated by immunohistochemistry, using antibodies that recognize lymphocytes. RESULTS: rAAV-angiostatin injection led to sustained expression of the angiostatin gene in chorioretinal tissue for up to150 days. FA analysis revealed significant reduction of the average sizes of CNV lesions in rAAV-angiostatin-injected eyes when compared with rAAV-lacZ-injected eyes at both 14 ($P = 0.019$) and 150 ($P = 0.010$) days after injection. Moreover, histologic analysis of CNV lesions also revealed significantly smaller lesions in rAAV-angiostatin-injected eyes ($P = 0.004$). As for adverse effects, rAAV-angiostatin injection did not cause inflammation or apoptosis of cells in retina and choroid. CONCLUSIONS: This is the first report that subretinal injection of rAAV-angiostatin can significantly reduce the sizes of CNV lesions. This and the absence of apoptosis and inflammation in chorioretinal tissue indicate the feasibility of a gene therapy approach for treatment of CNV disease.