BACTERIAL SEPSIS INCREASES SURVIVAL IN METASTATIC MELANOMA: *CLAMIDOPHYLA PNEUMONIAE* INDUCES MACROPHAGE POLARIZATION AND TUMOR REGRESSION *IN VIVO*

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Background

It has been recognized for over 100 years that cancer patients might recover following bacterial infections. Notoriously, William B. Coley induced erysipelas by local injection of streptococcal cultures in a patient bearing lymphoma. Surprisingly, decreased tumor volume and prompt improvement of patient's general condition were observed.

Our studies were initiated by a case of unexpected complete metastatic melanoma remission observed at our clinic in a patient who suffered sepsis syndrome during BOLD chemotherapy. After targeted antibiotic treatment and chemotherapy, the patient has become and remained completely asymptomatic and PET/CT-verified metastasis-free from 2009 to this date. The overall survival of stage IV melanoma is very poor even today. Since our patient has had 56 months disease-free survival, it seems unlikely that short-term BOLD therapy alone accounted for the complete recovery.

Methods

To reproduce the infection-induced tumor regression, the B16 melanoma model was employed which is characterized by reproducible lung metastasis development after i.v. tumor injection. Mice bearing B16F1 melanoma metastases were treated with heat-inactivated *Chlamydophila pneumoniae (C. pneumoniae),* an intracellular pathogen detected retrospectively in tissue sections of the patient. *C. pneumoniae* inhalation resulted in a significant immune cell infiltration involving even the lung metastases.

Results

The bacterial treatment significantly improved the general condition and survival of the animals. In accordance, based on histology, chemokine and cytokine profiling, we demonstrated an anti-cancer macrophage polarization. Additionally, heat inactivated *C. pneumoniae* depleted the melanoma growth factor CXCL1 both *in vivo* and *in vitro*.

Conclusions

We present the first evidence that *C. pneumoniae* treatment induces regression of mouse melanoma metastasis via macrophage polarization and depletion of melanoma growth factor CXCL1. Similar mechanisms may contribute to the unexpected recovery of our melanoma patient suffering from sepsis, and may play a role in analogous cases described in the literature.

A téma elméleti jellegű és előadást kívánok tartani.