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Effect of endostatin on preventing postoperative progression of distant metastasis in a murine lung cancer model

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ABSTRACT

Aims and background. The relapse and metastasis of cancer remain a predominant cause of death after surgical removal of the primary tumor. There is a positive linkage between the postoperative upregulation of systemic angiogenic activity and distant tumor metastasis. In the present study, we established a spontaneous metastasis model and investigated whether antiangiogenic therapy using endostatin could prevent the progression of distant metastasis after removal of the primary tumor.

Methods. Female C57BL/6 mice were implanted subcutaneously with 1×10^6 Lewis lung cancer cells. Twenty days after implantation of the cancer cells, the primary tumor was removed and the mice were randomly divided into three groups. The NS group received normal saline, the L-ES group received 3 mg/kg endostatin, and the H-ES group received 20 mg/kg endostatin intravenously daily for 10 days. The effect of endostatin on lung metastases and the survival time of the mice were observed. Flow cytometry and immunohistochemistry were carried out to assess the angiogenic activity. The serum endostatin levels in peripheral blood were measured using an enzyme-linked immunosorbent assay.

Results. The mean number of metastatic pulmonary nodules and the mean net lung weight in the NS, L-ES and H-ES groups was 10.2, 2.8 and 4.0, and 0.55 g, 0.31 g and 0.36 g, respectively. The difference between the NS group and the endostatin-treated groups was statistically significant (P <0.05). The endostatin-treated mice showed prolonged overall survival (P <0.05). Compared with the NS group, the endostatin-treated groups had lower levels of circulating endothelial cells in peripheral blood and showed a decrease in microvessel density in the metastatic tumors, with a more marked reduction in the L-ES group (P <0.05). The systemic presence of endostatin was gradually increased with the continued administration of endostatin to the mice.

Conclusions. Antiangiogenic therapy with endostatin is effective in inhibiting the postoperative progression of distant metastasis.

Key words: endostatin, remote metastasis, postoperative progression, lung cancer model.

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