01. IMMUNOTHERAPY OF HUMAN GLIOBLASTOMA MULTIFORME USING OK-432, AN IMMUNE STIMULANT. THE DETECTION OF TUMOR-DERIVED IMMUNE SUPPRESSOR(S)


*Department of Pharmacology, and **Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700

ABSTRACT

Approximately 20 new cases of glioblastoma multiforme have been diagnosed annually at Siriraj Hospital. Glioblastoma multiforme is the most invasive of the astroglial neoplasms with a tendency to spread widely throughout the brain. Glioblastoma is very often extensively spread by the time of diagnosis, leading to unresectability, inadequate local control and a consistently poor prognosis. The length and quality of survival have improved only minimally through neurosurgical technique, radiotherapy and chemotherapy. Radical surgery and radiotherapy remain the cornerstone of treatment. A very modest contribution is added by conventional chemotherapy. Therefore, a novel therapeutic model is required for this cancer. We proposed that OK-432, a heat-treated and penicillin-treated lyophilized powder of the Su substrain of Streptococcus pyogenes A3, could be used as an immunomodulating agent to treat this cancer. It has a biological response modifier like BCG. Addition of OK-432 to peripheral blood mononuclear cells (PBMC) of these patients should result in the enhancement of NK cell activity and autologous tumor killing activity. We measure the proliferation of PBMC in the present or absence of cultured autologous tumor cells. We found that OK-432 enhanced the proliferation of PBMC and this proliferation was suppressed in the presence of tumor cells in a dose-dependent relationship. This immune suppression is probably caused by tumor-derived immunosuppressors or by toxic metabolites excreted from tumor cells. Additional experiments will be performed to verify the nature of this immunosuppressor. Future therapeutic model may aim at the strengthening of immune system bypassing this suppression.