

Gaojushen a novel anti-cancer drug prepared from SEC superantigen

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1 Clinical observations

Gaojushen is a novel anti-cancer drug developed by Xiehe Bi-pharmaceutical Company, Shenyang China. It is prepared and processed from the filtrate of *Staphylococcus aureus* culture. The active component contained in it has been shown to be a SEC superantigen that is a metabolite of the culture. This superantigen is marked by its ability to stimulate T cells at a high frequency, thereby giving rise to potent cell-mediated immunological responses and producing a large variety of cytokines with the final result of apoptosis of tumor cells. The drug was approved for trial production in 1994 by the Center of the State Evaluation and Review of New Drugs, China, and was licenced for marketing by 1996 after finishing the phase III clinical trial.

Gaojushen has been proven to be safe and effective over the years of clinical use in tens of thousands of cancer patients. There is no evidence showing organ damage or decreases in white cell counts. The most common complaints are local erythema with pain after i.m. injection (ca 17% of cases) and mild to moderate fever of short duration (ca 12% of cases), otherwise there are no other untoward reactions.

Critical evaluation of 1000 cases of various types of cancer treated by the drug alone gives the results showing that the efficacy rate (CR + PR) (as judged by the criteria, i.e., regression of the tumor size, etc.) is 42.5% on average. However, the rate increases to 60% when combined with chemotherapy or radiation therapy. The drug is able to bring the white cell counts up to normal in patients with leukopenia un-

dergoing chemotherapy or radiation therapy. When used alone, it can relieve pain in 71.6% of cases and improve the quality of patients' lives in 88.7% of cases. In addition, the product is also the best choice for treatment of pleural effusion or ascites if such symptoms occur in cancer patients. It causes a rapid dissipation of accumulated fluid in about 76% of cases. In selected cases of cancer, such as nasopharyngeal or lung cancer, the efficacy is especially prominent. CR + PR rate may reach as high as 90.5% when combined with radiation therapy.

2 A brief account about its history of development

In the mid-1980s, an event that touched off our thought to develop Gaojushen was the observation of a case of lung cancer in a hospital in Shanghai. During hospitalization, the patient unexpectedly developed *Staphylococcus aureus* septicaemia. After the complication was controlled by strenuous efforts involving treatment with various antibiotics for a prolonged period of time, the tumor mass became progressively regressed and finally disappeared. The patient left hospital without any sequelae or recrudescence of tumor growth and metastasis. Such an unheard-of fantastic story in medical science attracted our great attention and interest. It is therefore reasonable to assume that there must be a relationship between the tumor growth and staphylococcal septicaemia, and it is possible that a certain active ingredient which inhibits tumor growth might be found either within the bacterial cell wall itself or in the culture filtrate as a metabolite.

These preliminary ideas prompted us to take a series of steps to explore what is the crux of the matter. Results from animal experiments obtained in 1990 showed that it was the culture filtrate that contained the active component. The most important findings were

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1. the culture filtrate could stimulate to a large extent the cell-mediated immunological responses; 2. it had a remarkable activity to inhibit tumor growth both *in vivo* and *in vitro*; and, 3. in particular, it could increase the white cell counts.

In 1992 and soon afterward, successful laboratory experiments finally revealed that 1. the active component contained in the filtrate was a superantigen of staphylococcal enterotoxin C (SEC) and, 2. the nature of the superantigen was further verified by its ability to

induce production of cytokines in a great quantity in the presence of peripheral blood monocytes and Sendai virus or human Namalwa cells of lymphoblast cell line plus Sendai virus.

In conclusion, 1. the use of Ganjushen for treatment of cancer has a sound theoretical basis because superantigen is the most powerful cell-mediated immunogen ever found to date, and 2. Ganjushen is the first superantigen-based anti-cancer drug put into practical use as far as we know.

N. B.: This is a lecture note delivered at a conference which was held in Rutgers University and also in MIT, USA, in August 2000. The original commercial name has been known as HAS.