

Clinical Evaluation of Immune Response in Patients with Cancer

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Immune response was clinically evaluated in 25 patients with carcinoma compared with 26 of non cancer patients by means of lymphocyte transformation against PHA which was shown as stimulation index.

In patients with cancer, stimulation index showed apparently as low as an average of 38 compared with 82 of non-cancer patients.

Furthermore, the level of stimulation index was a corresponding correlation to age in which low activation was presented in the elderly.

According to diseased organs, the weak response of stimulation index against PHA were observed in patients with the carcinoma of the esophagus and the lung.

The response of skin test for PPD, PHA, SK-SD and candida were inhibited in patients with advanced cancer of stage III and IV compared with that of stage I and II.

These responses were also suppressed in postoperative course until at least 6 months after surgery.

From these results, it was noted that operative procedures provoked the induced weakness against host defense immunologically.

However, it was certified that the use of immunopotentiator facilitated the activity of immune response during postoperative period for the patients with no severely advanced lung cancer of stage I and II despite of little effects for patients with advanced lung cancer of stage III and IV.

It was concluded that immune response of patients with cancer was inhibited by advancing carcinoma and by operative procedures but the use of immunopotentiator was beneficial to promote the host defense during postoperative period.

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INTRODUCTION

On recent advances in immunology, immunological knowledge has been utilized in the treatment for patients with malignant disease.

In general, surgical treatment is advocated for treatment of malignant disease in order to expect a suitable results preferentially. However, it was documented by many investigators that complete excision with extended resection did not necessarily resulted in permanent cure without distant metastasis and recurrence. In addition, reliability of combined therapy with adjuvant therapy has been substantiated by follow-up study clinically.

Furthermore, it has been noted immunologically that host defensive mechanism against malignant diseases plays an important role to enhance the curability and to prevent from recurrence.

The effects of various kinds of drugs and procedures, by which immunological activity of tumor bearing host might be provided, have been widely evaluated with further accuracy according to advance of immunology.

In this study, immunological responses of tumor-bearing host were tested by PHA responsiveness, skin test against PPD, SK-SD and candida. A comparison between immunological response and the degree of advancing disease by classification of clinical stage was made out in patients with cancer.

MATERIAL

Twenty-five patients with cancer and 26 patients without cancer, those who admitted in our department, were subjected to this study.

Lymphocyte transformation against phytohemagglutinin (PHA) was expressed by stimulation index, which was calculated from the following formula

$$\text{Stimulation index (SI)} = \frac{\text{cpm of lymphocyte with PHA}}{\text{cpm of lymphocyte without PHA}}$$

The values of stimulation index were compared between diseased organs and age distribution of cancer patients.

Furthermore, the reactions of skin test against PHA, PPD, candida and SK-SD were evaluated during preoperative and postoperative period by stage classification and diseased organ respectively.

In patients with lung cancer of stage II, the level of stimulation index against PHA were clinically observed during pre- and post-operative course up to 6 months following surgery.

In addition, the effects on administration of immunopotentiator were evaluated in the postoperative course which might contribute to promote the defensive mechanism by host mediation.

As a immunopotentiator, 2KE of OK432, 10mg of BCG twice a month, or PSK

every days were used after surgery in patients with lung cancer of stage II undergone radial lobectomy.

In addition, the magnitudes of responsiveness against PHA were tested in patient with lung cancer according to staging classification and also with elapse of the time after surgery.

RESULT

Stimulation index against phytohemagglutinin was shown according to age, compared with patients with or without cancer respectively in Fig I.

The values of stimulation index of patients with cancer was as low as an average of 38 while that of patients without cancer was as high as an average of 82.

Interestingly enough, an elderly patients over 60 years of age had low values of stimulation index in comparison with those of younger patients.

However, the values of stimulation index were low even in younger group with

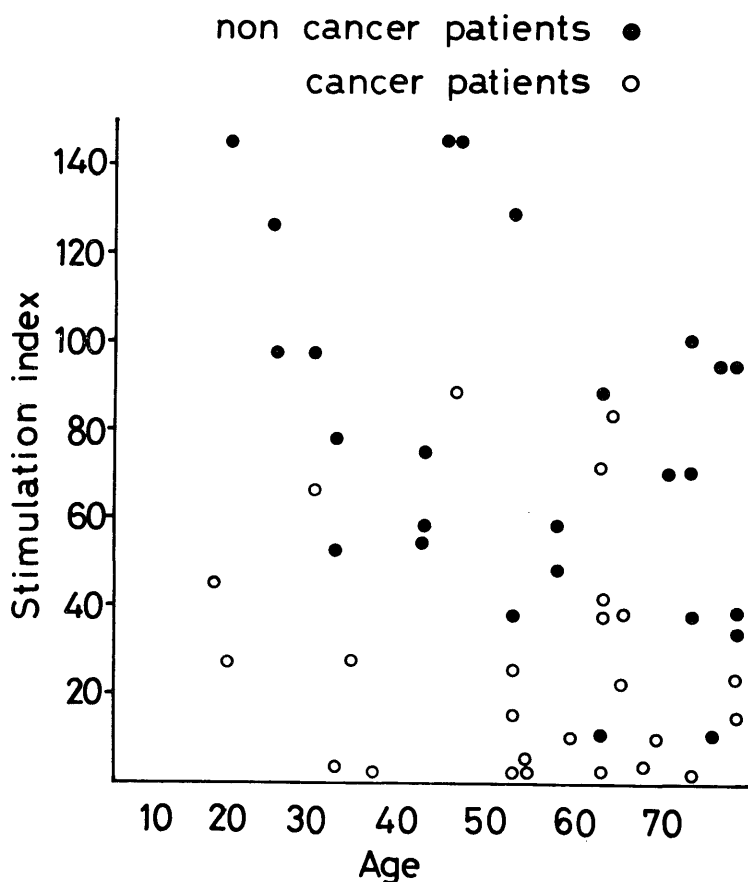


Fig 1. Relationship between stimulation index and age in patients with or without cancer.

cancer.

From these results, it was noted that stimulation index against phytohemagglutinin showed a tendency to be low in patients with cancer and also these tendency was prominent in younger patients.

Furthermore, the values of stimulation index against PHA was compared according to diseased organ as shown Fig 2.

In patients with lung cancer and esophageal cancer, the values of stimulation index against PHA showed extremely low compared with those of patients with gastric cancer.

It is considered from these results that there may be organ specificity from the view of immunologic response against PHA.

It seems that less response against PHA in patients with lung cancer and esophageal cancer rather than gastric cancer imply weak immunologic defense of tumor-bearing host.

The normal response against PHA by more than 80 of stimulation index has not been shown in patients with lung cancer and esophageal cancer, whereas the magnitude of PHA reaction in patients with gastric cancer has still maintained at low levels compared with non-cancer patients.

From the results of skin test against PHA, PPD, candida and SK-SD, positive ratio of skin test did not correlate between reactions against various kinds of antigen.

In patients with lung cancer of stage I and II, the majority of cases showed positive skin reaction while negative reactions of skin test were seen in patients of stage III and stage IV as shown in Fig 3.

It is apparent from above results that negative skin reaction was shown in advanced

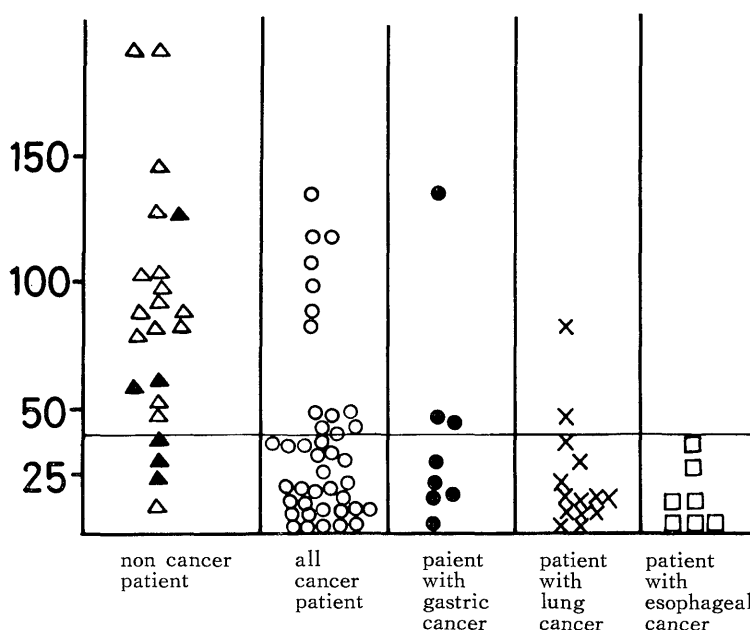


Fig. 2 Stimulation index according to diseased organ compared with non-cancer patients.

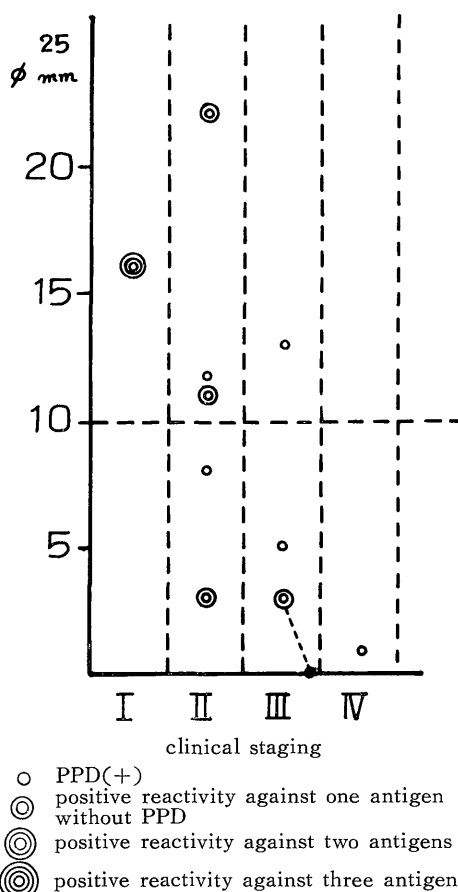


Fig 3. The preoperative response of skin test according to clinical staging of lung cancer.

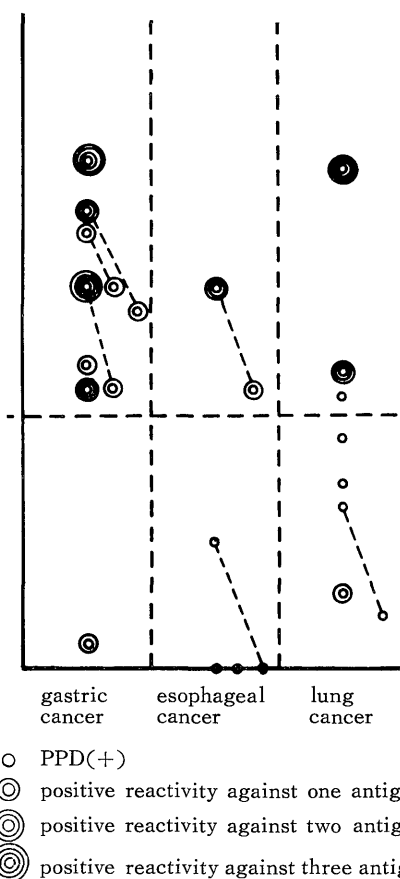


Fig 4. The response of skin test after surgery according to diseased organ. compared with postoperative period

cancer stage, reflecting weak immunological defense of tumor-bearing host.

The changes of reaction of skin test after surgery were mainly evaluated in patients with gastric cancer and esophageal cancer.

The degree of response by skin test showed the defined decreases within 1 or 2 months following surgery as shown in Fig 4.

However, skin test responsiveness did not so remarkably changed compared with pre- and postoperative stage.

In patients with lung cancer of stage II undergone radical lobectomy, the level of stimulation index against PHA decreased reflecting inhibition of immunological defense until at least 6 months following surgery.

In one of them, high responsiveness against PHA was shown in the course of postoperative period which received the inoculation of BCG.

There were not found out any differences with special reference to effectiveness of immunomanipulation between BCG, OK-432 and PSK of immunopotentiator against

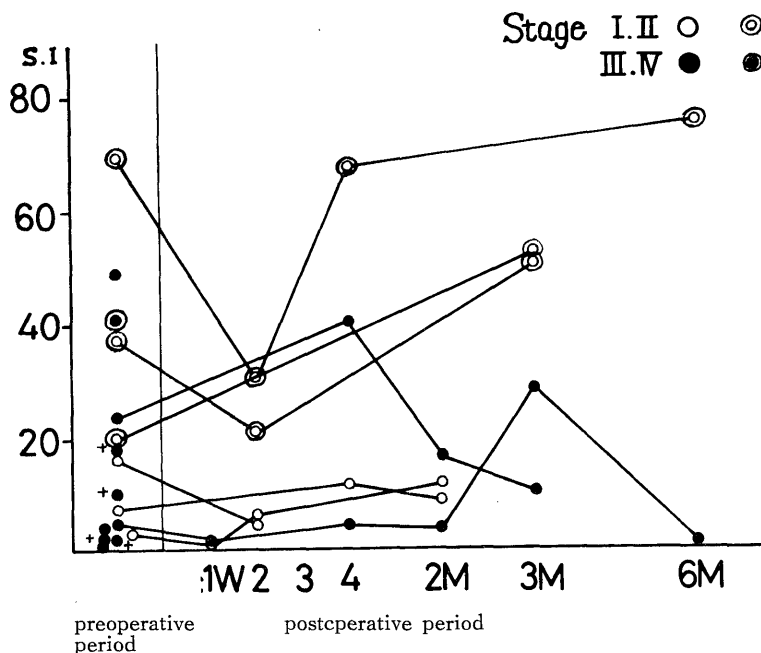


Fig 5. Postoperative changes of stimulation index for patients with lung cancer of stage I or II and stage III or IV used OK-432

the patients with lung cancer of stage II.

According to advancing disease of lung cancer, the responsiveness against PHA were apparently depressed.

In patients with stage I and II of lung cancer, the administration of OK-432 produced high responsiveness against PHA in the postoperative course, whereas the effectiveness of immunopotentiator was not necessarily presented in advanced cases of stage III and IV as presented in Fig 5.

From above results, it was noted that the immunological responsiveness in patients with far advanced cancer was not accelerated by immunopotentiator.

COMMENT

The immune responses of tumor-bearing host has been considerably defined at the cellular level in experimental animals as well as in human beings according to advance of immunology.

It has been ascertained that these immunue responsiveness was also correlate to the degree of advancing cancer.

In this study, the responsiveness against PHA was clinically tested in patients with or without cancer.^{1)~4)}

These responses were significantly inhibited in patients with cancer compared with

non-cancer patients.

Furthermore, it is obvious that these responses correlate to age.

In the aged group, the responsiveness against PHA were generally depressed, the majority of cases with cancer were detected in the elderly, therefore, the immunopotenti-ation necessitate to enhance the host defense immunologically.

According to affected organs by cancer, the patients with carcinoma of the esophagus and the lung showed a weaker magnitude of responsiveness against PHA compared with that of the carcinoma of the stomach.

Furthermore, immune response was evaluated by skin test against PPD, PHA, SK-SD and candida respectively. The responses against these reagens were observed as the same order of magnitude against each antigens.

There was not found out a perticular reagens which had a specificity for elective response of carcinoma.

Interestingly enough, the response by skin test showed the intimate correlation to classification of cancer stage. In patients with cancer of stage I or II, positive rate of skin test was still high in contrast to those with cancer of stage III or IV.

There is widespread interesting fact that the response of skin test decrease in post-operative course up to at least 6 months after surgery.

This reports provides the following results that the removal of tumor mass by surgery dose not necessarily result in immunopotentialiation against tumor-bearing host.⁵⁾

It is considered as a consequence that a trial treated by immunopotentiator is indispensable to improve the prognosis for patients with cancer following surgery.⁶⁾⁷⁾

In early postoperative period, the effectiveness of immunopotentiators such as OK-432, PSK and BCG was evaluated by means of the magnitude of the response against PHA.

The therapeutic effects of immunopotentiator was obvious in patients with cancer of stage I or II.⁸⁾

And the immune response against PHA was apparently facilitated by treatment of immunopotentiator, whereas the effects of immunomanipulation by OK-432, BCG and PSK were not always observed in patients with advanced cancer of stage III or IV.

As a result of these observations, it is emphasized that immunotherapy is beneficial in patient with no severely advanced cancer and with surgery.

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