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Effect of Long-term Administration of Immunomodulatory Food on Cancer Patients Completing Conventional Treatments

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Summary

A study was conducted to investigate the effects of long-term administration of the immunomodulatory food BioBran, rice bran arabinoxylan derivative, on 16 cancer patients, mainly in stage IV with various conventional lesions, who had just undergone conventional cancer treatments, such as surgery, chemotherapy and radiotherapy. The main clinical observations were the safety and effect of BioBran on the nutritional state of the patients, who were exhausted due to treatment. During the administration period, no decreases in body weight and leukocyte count or significant changes in leukogram were observed. Rather, the leukocyte count increased. In addition, most patients showed an increase in NK cell activity and a remarkable decrease in tumor markers.

Key words: complementary medicine, rice bran arabinoxylan derivative, immunomodulatory food, safety

Introduction

In our clinic, complementary medicine is used in cancer patients who completed surgery, chemotherapy, and irradiation therapy to improve QOL, prevent recurrence, and enhance life prolongation. We call the medicine "Ryo-yo." "Ryo" means treatment given in the clinic to enhance healing and immunity, and "yo" means daily cares by the patients themselves to increase their self-healing capacity. For daily care, patients are trained for breathing, diet, and physical and mental health[1]. The diet should be based on modern dietetics or grains and vegetables to enhance prophylactic power. Functional foods are also used as part of the diet therapy, but patients make the decision about ingestion. Many functional foods are used to prevent decreased immunity and to reduce adverse reactions in cancer treatment. All of our patients take 1-5 kinds of functional foods. Most of them contain ingredients equal or similar to those in foods taken every day. However, the form is concentrates and capsules, granules, or tablets of partially purified ingredients in most cases. Thus, there is a possibility of ingesting larger quantities of some ingredients than those contained in foods. As it is reported that excessive ingestion of β carotene promotes lung cancer[2], sufficient attention should be paid to safety. In the present study,

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the effect of long-term administration of BioBran, most frequently used by our patients, was evaluated in 16 cancer patients with nutritional problems who had just completed conventional treatments, especially focusing on the effect on leukocytes.

Table 1 Backgrounds of subjects

Initials	Age	Sex	Primary lesion	Study period
K.O.	56	Male	Stomach	January to July 2001
I.R.	64	Male	Large intestine	March to September 2001
M.T.	59	Male	Large intestine	March to September 2001
K.K.	44	Female	Breast	February to August 2001
T.H.	58	Female	Rectum	May to November 2001
F.A.	46	Female	Breast	July 2001 to January 2002
T.S.	60	Female	Stomach	August 2001 to February 2002
K.H.	47	Female	Breast	December 2001 to June 2002
E.I.	44	Male	Biliary tract at hepatic portal	February to August 2002
H.Y.	59	Female	Large intestine	February to August 2002
H.M.	77	Female	Ovary	December 2001 to June 2002
M.N.	72	Female	Thyroid gland	January to July 2002
Y.I.	44	Male	Lung	October 2001 to April 2002
Y.H.	84	Male	Rectum	January to July 2002
N.A.	39	Female	Uterine cervix	March to September 2002
K.M.	53	Male	Rectum	April to October 2002

Table 2　Changes in body weight (kg)

Initials	Before study	After study	Difference
K.O.	70.0	71.0	+1.0
I.R.	67.0	69.0	+2.0
M.T.	61.0	60.0	−1.0
K.K.	48.0	49.0	+1.0
T.H.	53.0	53.0	0
F.A.	49.0	51.0	+2.0
T.S.	38.0	38.0	0
K.H.	52.5	53.0	+0.5
E.I.	47.0	46.5	−0.5
H.Y.	50.0	51.0	+1.0
H.M.	44.0	44.0	0
M.N.	46.5	47.0	+0.5
Y.I.	64.0	65.0	+1.0
Y.H.	59.0	60.0	+1.0
N.A.	45.0	46.5	+1.5
K.M.	68.0	68.0	0

Table 3　Changes in leukocyte count and subsets

Initials	Leukocyte count (/mm^3)			Neutrophil (%)			Lymphocyte (%)		
	Before administration	After administration	Difference	Before administration	After administration	Difference (%)	Before administration	After administration	Difference (%)
K.O.	5500	6500	+1000	65.7	76.2	+10.5	24.9	19.5	− 3.4
I.R.	6100	4400	−1700	69.8	62.8	− 7.0	24.1	27.6	+ 3.5
M.T.	3500	4100	+ 600	56.4	59.5	+ 3.1	27.2	31.2	+ 4.0
K.K.	3400	3600	+ 200	60.8	64.9	+ 4.1	22.7	21.3	− 1.4
T.H.	5700	5400	+ 300	51.9	53.0	+ 1.1	42.0	42.5	+ 0.5
F.A.	2500	3000	+ 500	57.0	52.1	− 4.9	24.5	42.5	+18.0
T.S.	3800	4200	+ 400	40.0	55.3	+15.3	56.0	35.9	−20.1
K.H.	4800	4400	− 400	80.0	71.7	− 8.3	11.0	20.6	+ 9.6
E.I.	2800	3400	+ 600	57.9	67.0	− 9.1	25.6	23.8	− 1.8
H.Y.	4200	5400	+1200	50.5	61.9	−11.4	33.7	27.2	− 6.5
H.M.	3000	3500	+ 500	54.6	63.8	+ 9.2	30.3	29.9	− 0.4
M.N.	7300	6000	−1300	68.9	62.2	− 6.7	24.6	28.7	+ 4.1
Y.I.	3700	5600	+1900	71.7	82.0	+10.3	19.7	11.5	− 8.2
Y.H.	5600	5800	+ 200	64.0	64.2	+ 0.2	25.2	23.5	+ 1.7
N.A.	5200	4300	− 900	80.0	71.1	− 8.9	13.5	14.2	+ 0.7
K.M.	5300	5900	+ 600	44.8	48.8	+ 4.0	35.7	23.6	−12.1

Table 4 Changes in leukocyte count and subsets from the normal ranges

	Leukocyte count		Neutrophil		Lymphocyte	
	Before administration	After administration	Before administration	After administration	Before administration	After administration
L	7	4	-	-	11	13
N	9	12	8	5	4	3
H	-	-	8	11	1	-

Table 5 Categorization of changes in leukocyte count and subsets

	Leukocyte count	Neutrophil	Lymphocyte
Increase	9	5	2
No change	4	5	10
Decrease	3	6	4

Figure 1 Changes in NK activity

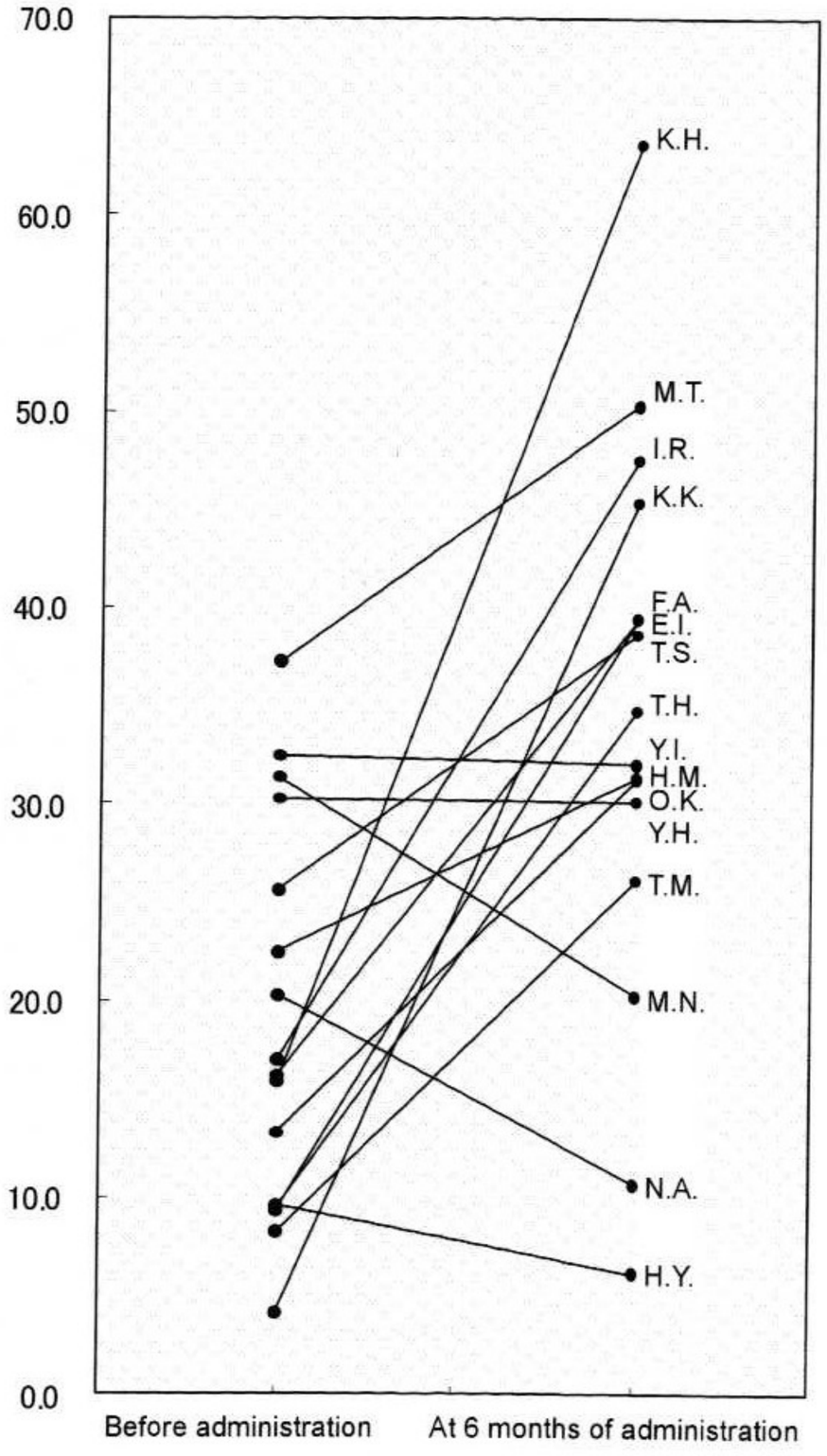

Table 6 Changes in NK activity

Patient's initials	Before administration	At 6 months of administration
K.O.	13.3	31.2
I.R.	17.0	47.5
M.T.	37.2	50.3
K.K.	4.1	45.3
T.H.	9.5	34.8
F.A.	9.3	39.5
T.S.	25.6	38.6
K.H.	15.9	63.6
E.I.	16.2	39.4
H.Y.	9.6	6.1
H.M.	22.5	31.4
M.N.	31.4	20.3
Y.I.	32.4	32.0
Y.H.	30.3	30.2
N.A.	20.3	10.7
K.M.	8.2	26.2

Methods

1. Patients and study period

The subjects were 16 cancer patients who met the criteria (1) to (3) below, and the study period was 6 months.

Table 1 shows the age, primary lesion, and study dates for each patient.

1) Cancer patients just after completion of surgery, irradiation therapy, and/or chemotherapy

2) Patients visiting this clinic for observation of outcome and care to improve QOL and prevent recurrence

3) Patients who consent to ingest BioBran at 3 g/day.

2. Study items

The study items were body height and weight, leukocyte count and subsets (neutrophils, lymphocytes, monocytes, eosinophils, basophils, and band cells), NK activity, tumor markers, adverse reactions (abdominal pain, vomiting, and an enlarged feeling in the abdomen), and interruptions of administration and the reasons for interruption.

Height was measured at the start of the study. Body weight and leukocyte count and subsets were checked 3 times at the start of, during, and at the end of the study. NK activity and tumor markers were determined every month. Adverse reactions and interruptions of ingestion were checked throughout the study period.

3. Rice bran arabinoxylan derivative (BioBran)

The study substance BioBran is produced by partially hydrolyzing rice bran extract with many carbohydrases. There are many reports on the physiological actions of MGN-3, the generic name of BioBran, such as immunomodulation[3-4], active-oxygen scavenging[5], blood sugar control[6] and reduction of adverse reactions to anticancer drugs[7].

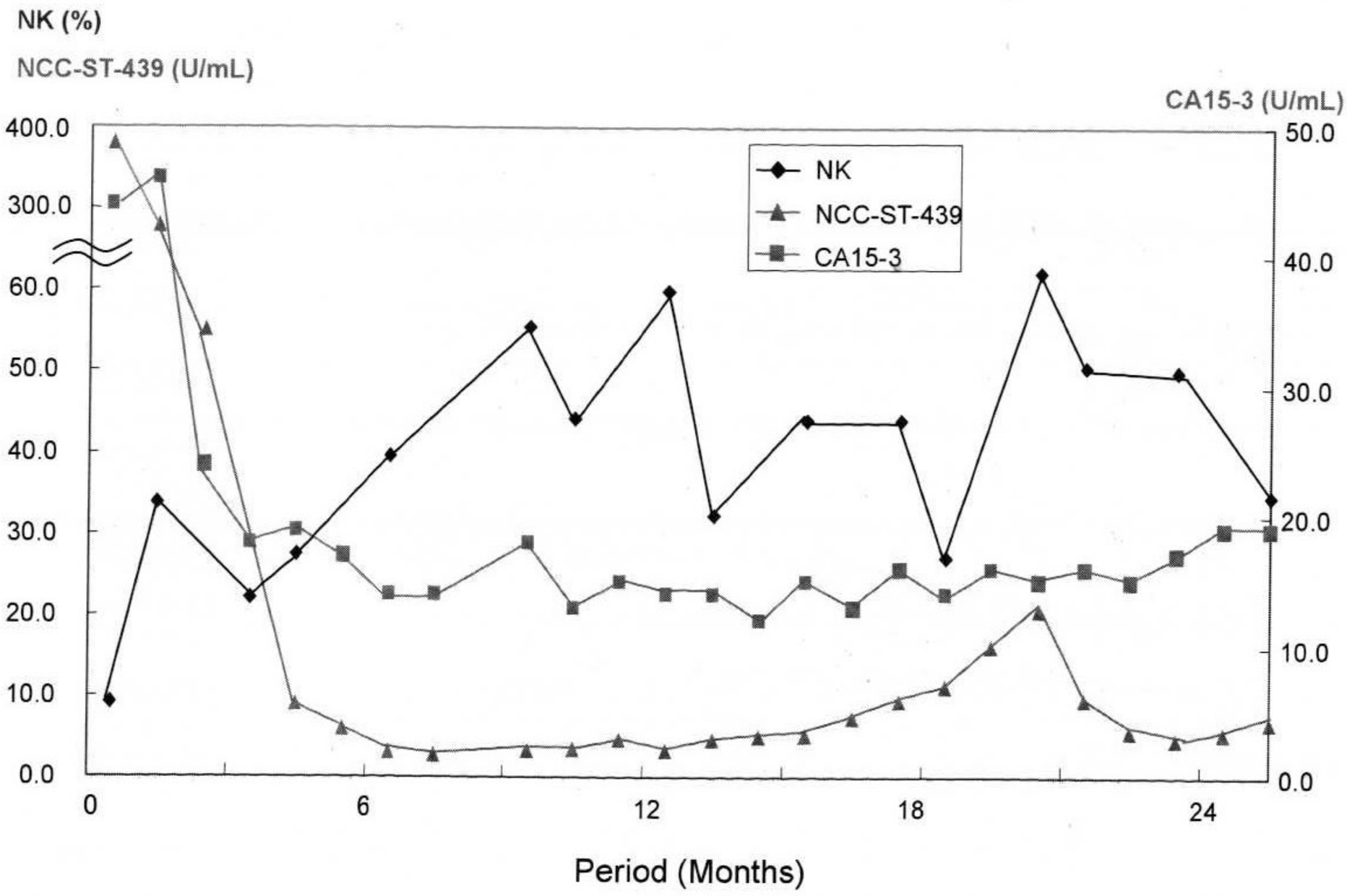

Figure 2 Breast Cancer (Stage IV) F.A. (46) F.

Results

All 16 subjects completed the administration of BioBran continuously during the study period.

1. Changes in body weight

Body weight increased in 10 patients, decreased in 2, and was unchanged in 4. The range of change was within 4% for both increase and decrease. BioBran had almost no effect on body weight. Table 2 shows changes in body weight.

2. Changes in leukocytes

Changes in leukocyte counts and subsets were studied. Table 3 shows leukocyte counts and results for neutrophils and lymphocytes. The normal range is 4000-9000/mm^3 for the leukocyte count, 40%-60% for the neutrophil fraction, and 30%-45% for the lymphocyte fraction. Individual measurements before and after administration were divided into the categories of H (higher than the normal ranges), N (within the normal ranges), and L (lower than the normal ranges) (Table 4).

The changes in measurements were classified into the categories of increase (changes above 10% for leukocyte counts and 5% each for neutrophil and lymphocyte fractions), no change (changes within ±10% and ±5% each, respectively), and decrease (changes under -10% and -5% each, respectively) (Table 5).

The leukocyte count was generally low in the subjects of this study because they had just completed conventional treatments: it was below the normal range in 7 of 16 patients (44%).

After 6 months of BioBran administration, the leukocyte count increased in 9 of 16 patients, and 3 of them had a normal value. The fraction of neutrophils increased slightly, but no constant trend was observed. The lymphocyte fraction was low, and there was almost no change before and after administration. In 1 patient each, however, the value changed from a low level to the normal range and from a high level to the normal range. Overall, changes towards a healthy condition were observed, but no adverse changes were noted in the leukocyte profile for 6 months.

3. NK activity and tumor markers

The NK activity at the start of the study was ≤ 30% in 11 patients, 30%-50% in 3, and ≥ 50% in 2, and the rate of patients with normal NK activity was 19%. After administration of BioBran, the NK activity tended to increase, and 11 patients (69%) had a normal NK activity. Tumor markers decreased in 10 (63%) after administration of BioBran.

Figure 1 and Table 6 show changes in NK activity.

4. Adverse reactions

No adverse reactions to BioBran were observed and reported by any patient.

5. Cases who had marked improvement in nutritional state

1) Patient initials: F.A., female, 46 years, recurrent breast cancer (stage IV)

The patient received a diagnosis of breast cancer in July 1998 and underwent surgery and hormonal treatment. After 2 years and 6 months, she had metastases in the left iliac bone, lumbar vertebra, and uterine body. A hysterectomy was performed and Taxol and Paraplatin given for bone metastases. However, no improvement was observed, and metastases to the thoracic vertebrae and ribs occurred. She visited our clinic in July 2001, when the tumor markers CA15-3 and NCC-ST-439 were at high concentrations of 44 U/mL and 369 ng/mL, respectively, and the NK activity was at a low level of 9.3%. She had malaise, severe bone pain, and low QOL (PS2). She received our therapy while continuing administration of Paraplatin. BioBran was taken at 3 g/day. The NK activity increased to 33.7% at 1 month, and the levels of two tumor markers decreased rapidly at 2 months. At 7 months, pain due to bone metastases disappeared and malaise was reduced. Now after 34 months (April 2004), she lives a normal life with QOL maintained (PS0) (Figure 2).

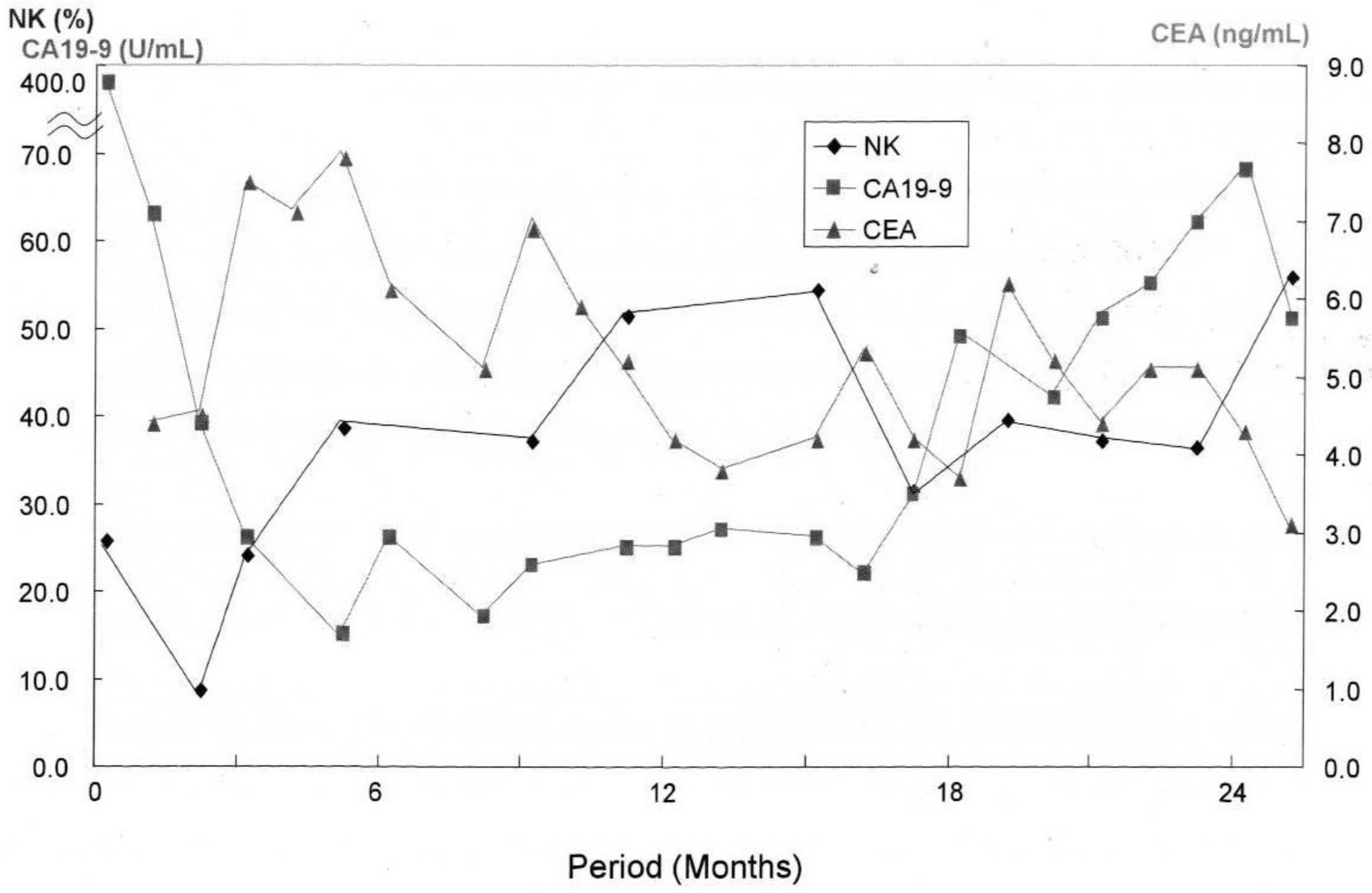

Figure 3 Stomach Cancer (Stage IV) T.S. (60) F.

2) Patient initials: T.S., female, 60 years, stomach cancer (stage IV)

The patient underwent an operation for scirrhous carcinoma of the stomach, but curative resection was impossible because of cancerous peritonitis. She visited our clinic in August 2001 and complained of abdominal pain, an enlarged feeling in the abdomen, anemia, and anorexia (PS1). She was given the oral anticancer drug TS-1 and our hospital's therapy. BioBran was taken at 3 g/day. The level of CA19-9 was 390 (U/mL) at the first visit and reduced within the normal range at 3 months. The level of CEA increased, but began to decrease at 6 months. Subjective symptoms gradually improved. Now at 33 months (April 2004), her nutritional state is good, and she lives a normal life (PS0) (Figure 3).

Discussion

During administration of BioBran, the patients' nutritional state was good, and they had no exacerbation in subjective and objective symptoms. Overall improvement was observed. The leukocyte count was low in many patients at the start of the study, but increased in almost all patients at the end of the study, and some had a normal value. Our clinic's complementary medicine maintains good physical conditions in high frequency after conventional cancer treatment. The conditions of patients in the present study were especially good, without a large difference in nutritional state between the patients and healthy people. The NK activity tended to increase: the number of patients with normal NK activity changed from 3 before the study to 11 after the study. These

results supported data reported from other institutions[8]. These phenomena were not clearly observed in patients who were not given BioBran.

Long-term administration of BioBran had no adverse effects like compromised immunity on cancer patients after conventional treatment, suggesting that BioBran is useful as a diet therapy that assists the improvement of the nutritional state.

Conclusion

Long-term administration of BioBran caused no subjective or objective adverse effect in cancer patients with decreased immunity. Improvement, rather than adverse changes, was observed in leukocyte counts and subsets. The NK activity decreased at the baseline, but normalized after administration.

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